THE American Journal OF Gastroenterology

VOL. 29, NO. 2 FEBRUARY, 1958

Twenty-third Annual Convention
New Orleans, Louisiana
19, 20, 21, 22 October 1958

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AMERICAN COLLEGE
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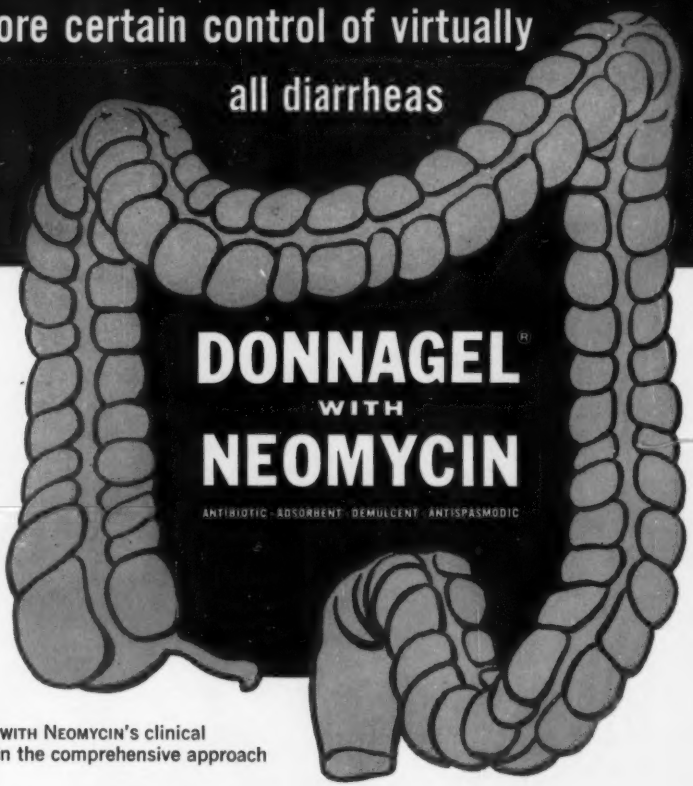

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1. Cayer, D.; Sohmer, M.F., and Sugg, W.C.: The Effect of Prolonged Continuous Therapy on the Course of Chronic, Recurring Peptic Ulcer; Anticholinergic Therapy with SKF-4740 ('Darbid'), North Carolina M.J. *18*:311 (Aug.) 1957.

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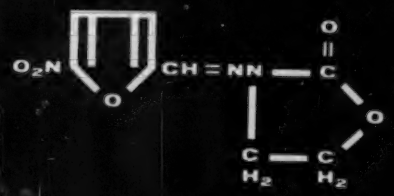

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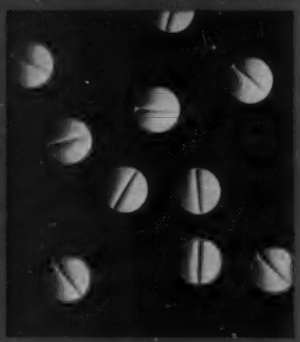

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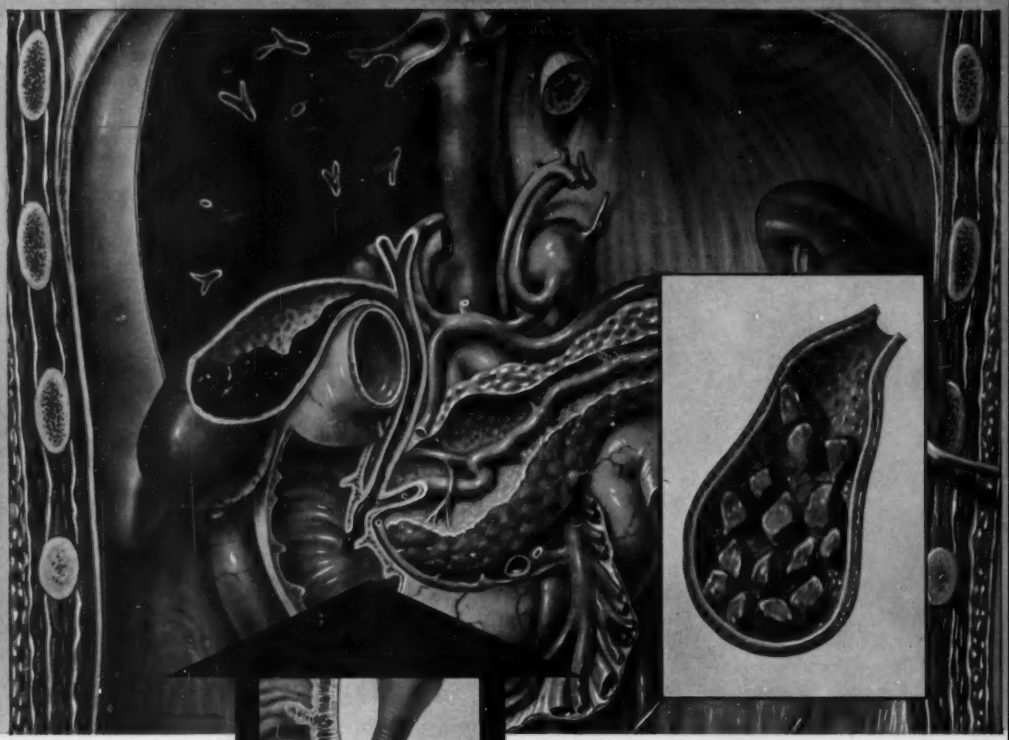

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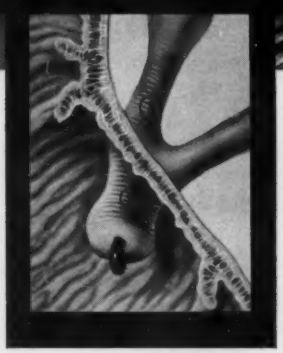

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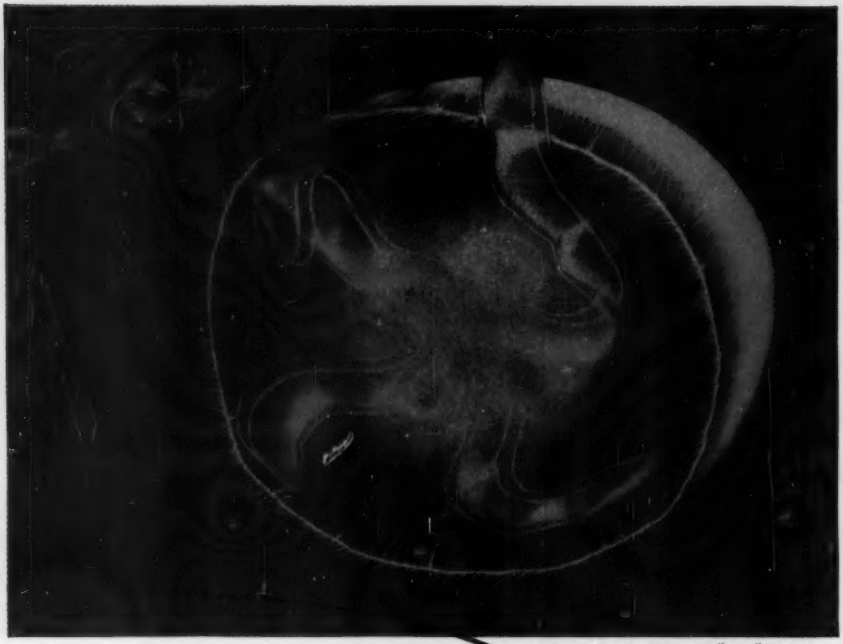

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VOLUME 29 FEBRUARY, 1958 NUMBER 2

CLINICAL ASPECTS OF BACTEROIDES INFECTIONS IN GASTROENTEROLOGY*

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INTRODUCTION

Recent textbooks on general medicine and its various specialties scarcely mention *bacteroides* although it is a common genus. The explanation lies in the fact that *bacteroides* is not only difficult to isolate, but even more difficult to define precisely. Its biologic reactions are extremely hard to observe, for it does not grow readily on differential media. The genus *bacteroides* is usually defined as a gram-negative, nonsporing anaerobic bacillus which is almost invariably found in any foul-smelling material such as a gangrenous appendix or a liver abscess.

The first report concerning *bacteroides* is found in a German medical journal in 1884 by Loeffler. He was able to produce necrotic lesions in mice by subcutaneous inoculation of diphtheritic membranes obtained from calves. Although foreign literature cites work done in the field of *bacteroides* after Loeffler, it is not until 1901 that we find a significant report published in the United States.

A complete review of the literature on *bacteroides* in gastroenterology plus its morphology, cultivation, agglutination reactions, enzyme reactions, bio-

*Read before the 22nd Annual Convention of the American College of Gastroenterology, Boston, Mass., 21, 22, 23 October 1957.

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chemical reactions, animal pathology—as well as complete classifications—can be found in the thesis entitled "Bacteroides in Gastroenterology" (SHR) on file at the Department of Microbiology , University of Chicago, June, 1957. Time does not permit including these subjects in this paper.

Normal Habitat of Gastrointestinal Tract and Predominant Organism

It is interesting to note the uniformity of the findings of scientists investigating the presence of *bacteroides* in the normal adult stool. In 91 per cent of 60 studies of adult stools, Eggerth and Gagnon (1933) reported that the predominating organism was *bacteroides*. Weiss and Rettiger (1937) confirmed the observations of Eggerth and Gagnon and concluded that the *bacteroides* is the predominant organism in the intestines of most human beings. In 90 per cent of the stools studied, Misra (1938) found a marked preponderance of the obligate anaerobes which appeared to be members of the *bacteroides* group. He suggested more intensive study to determine what role, if any, this organism plays in normal and abnormal conditons. Dragstedt, Dack, and Kirsner (1941) stated that the *bacterium necrophorum* (the name they preferred to *bacillus funduliformis*) was probably present in the normal alimentary tract of man and monkey.

Major Pathological Conditions Associated with the Field of Gastroenterology

Bacteremia:—Thompson and Beaver (1932) reviewed ten cases of bacteremia caused by *bacteroides,* and added two cases of their own. By 1936, we find a growing awareness of the importance of *bacteroides* in man. The 27 June 1936, issue of the *Journal of the American Medical Association* carried an editorial on the subject, stressing *bacillus funduliformis* as a saprophyte of the appendix. Thus a localized inflammation of this organ may result in anaerobic septicemia. The editors concluded that there should be, in the United States, more frequent recognition of the possibility of *bacteroides* septicemia.

As further evidence that *bacteroides* was being considered more and more important in medicine, Dixon and Deuterman (1937) recommended blood cultures for *bacteroides funduliformis* in cases of icterus following surgery, even though evidence of septicemia might be lacking. Early blood cultures for anaerobic bacteria were believed to be necessary in order to make an antemortem diagnosis.

In a report of 20 cases of *bacteroides* infections at the Massachusetts General Hospital (1939-1943) Smith and Ropes (1945) described one case of septicemia arising from an abdominal abscess.

Ruys (1947) reported a pure culture of *bacteroides funduliformis* obtained twice from the blood of a fatal case of sepsis associated with a primary diverticulitis. The culture was obtained in tarozzi liver broth.

All evidence points to the fact that *bacteroides* septicemia should certainly be considered in cases having a septic course associated with various gastrointestinal diseases.

Association with carcinoma of the colon:—Six cases of *bacteroides* infections following surgery for cancer of the colon were cited by Dixon and Deuterman (1937). Mortality rate was 83 per cent, with multiple liver abscesses noted in every patient in which death occurred. The authors agreed that ulcerating necrotic cancer provided an ideal habitat for the proliferation of the *bacteroides* organism.

Two cases are reported by Beigelman and Rantz (1949). The first case showed a large abscess (*bacteroides*) adjacent to a highly malignant retroperitoneal sarcoma. Death, however, was attributed to the highly malignant lesion. The second case showed an abscess *(bacteroides)* adjacent to an inoperable rectal cancer.

The possibility should be consdered of *bacteroides* infection contributing to a rapid down-hill course in cases of malignancy.

Achalasia of the esophagus associated with pulmonary and hepatic abscesses:—A case in point is one discussed by Fischer and McKusick (1953). A patient with aspiration pneumonia of the right lower lobe, plus a dilated esophagus, developed septicemia. In spite of subsequent hepatic abscesses and hepatitis, the patient recovered after courageous therapy.

Perforation of gastrointestinal tract:—Smith and Ropes (1945) published an account of three cases of peritonitis resulting from ruptured appendices, and one case of peritonitis arising from salpingitis. They concluded that, despite the fact that *bacteroides* was cultivated from the peritoneum, this did not confer an unfavorable prognosis.

One case of appendicitis followed by intraabdominal abscesses was described by Beigelman and Rantz (1949).

Among the cases reported by Fischer and McKusick (1953) were two of perforation. One had abdominal abscesses with chronically draining sinuses, probably due (but not proved) to *bacteroides* infection. The other was a case of acute appendicitis combined with abdominal abscesses. In the latter, *bacteroides funduliformis* was isolated. Both patients recovered with adequate therapy.

If we accept the fact that *bacteroides* is present in a high percentage of stools, then it is not surprising that it should be common in the peritoneum

when leakage from the bowel has occurred. Usually the infection is mixed, with anaerobic streptococci, particularly of the nonhemolytic variety, being frequently associated with the *bacteroides.*

Liver abscesses:—Beaver, Henthorne, and Macy (1934) gave a classic description of liver abscesses caused by *bacteroides funduliformis.* The abscesses were large and usually multilocular. The exudates varied from thick and tenacious to caseous, and ranged in color from white to yellow or greenish-yellow. A peculiar odor resembling butyric acid was associated with the exudates. Usually the abscesses were well encapsulated by fibrous tissue. Polymorphonuclear neutrophilic leucocytes predominated.

In 1945 an interesting case of *bacteroides* liver abscess following colectomy was cited by Smith and Ropes. Two cases of cholangitis with liver abscesses due to *bacteroides funduliformis* were reported: one by Rubin, Bornstein, Perrine, Schwimmer, and Rubin (1951), and the other by Fischer and McKusick (1953). In both instances, the patients recovered.

Six cases of *bacteroides* infections originating from the gastrointestinal tract were described by McVay and Sprunt (1952). Icterus was observed in all cases, and hepatic abscesses were demonstrated in all, either by surgical procedures or at necropsy. In spite of the fact that the six patients were well-nourished and well-developed on admission, four died.

It is important to distinguish the *bacteroides* abscesses from the amebic abscesses, actinomycotic abscesses, or abscesses due to other pyogenic microorganisms, particularly staphylococci and streptococci. Grossly, on superficial examination, they may appear to resemble one another. There are, however, definite distinguishing features. Amebic abscesses are usually solitary and unilocular. Actinomycotic abscesses usually have a heavy fibrous and granulomatous capsule, plus associated sinus tracts. Staphylococcic and streptococcic abscesses are multilocular and have a honeycomb appearance, similar to that of actinomycotic abscesses. The staphylococcic and streptococcic abscesses, however, are more often associated with suppurative pylephlebitis. In the end, the final diagnosis is dependent on microscopic and bacteriologic examination.

Chronic ulcerative colitis:—To a very great extent, the literature associating *bacteroides* with chronic ulcerative colitis has emanated from the University of Chicago.

In a study of 15 cases of nonspecific ulcerative colitis, Dack, Dragstedt, and Heinz (1936) reported *bacterium necrophorum* to be the predominant organism in the isolated colons of three of these patients. The organism persisted in large numbers as long as the colons remained severely diseased. In the remaining 12 patients, the colons were nonisolated, but the authors were able to culture *bacterium necrophorum* from seven of them. The organism also was demonstrated in two cases of specific ulcerative colitis.

The following year Dack et al described a child with chronic ulcerative colitis who, at autopsy, was found to have a large thrombus in the liver, plus small thrombi in some of the colic vessels. The predominant organism in the liver thrombus was *bacterium necrophorum*. Up to this time it was believed that no other experimenters had associated *bacterium necrophorum* with chronic ulcerative colitis.

In 1938, Dack, Dragstedt, Johnson, and McCullough indicated that both *bacteroides funduliformis* and *bacterium necrophorum* were associated with necroses of mucous membranes in men and animals, with resultant metastatic abscesses. Dack et al, however, decided to retain the name *bacterium necrophorum*, since the strain variations and the differences in degree of pathogenicity were not sufficient to differentiate between the species.

A paper written for the American Surgical Association meeting in April, 1941, by Dragstedt, Dack, and Kirsner leads one to believe that *bacterium necrophorum* may play an etiologic role in chronic ulcerative colitis. This conclusion was based upon two facts: 1. *bacterium necrophorum* was the predominant organism in the isolated colon during exacerbation of the disease, and tended to disappear with remission; 2. specific antibodies for *bacterium necrophorum* were demonstrated in the blood in cases of chronic ulcerative colitis, but not in the blood of well individuals.

In the discussion period following this paper, Dr. Frank L. Meleney, New York City, confirmed the statement of Dragstedt that the organism was very susceptible to oxygen. Yet he stated that his group could find *bacterium necrophorum* in only 3 of 40 carefully examined ulcerative colitis cases.

In summarzing this group of papers, it would seem that after other factors or conditions break down the mucous membrane of the colon, then *bacteroides* is capable of continuing the pathologic process.

Pathogenicity of bacteroides melaninogenicus and its importance in surgical infections:—Characteristics of *bacteroides melaninogenicus* include the possession of a fibrinolysin, and the production of a putrid foul odor in cultures. Weiss (1943) proved that strains of this black pigment-producing organism recovered from human lesions were pathogenic for rabbits and mice. The surgical importance of the bacterium was evident in this paper. The cases were varied and Weiss was able to demonstrate the frequent association of *bacteroides melaninogenicus* with many lesions of the gastrointestinal tract.

Frequency of isolation of various bacteria from abdominal suppurative lesions:—Using 111 specimens of pus from abdomens, Gillespie and Guy (1956) discovered the *bacteroides* group to be present in larger numbers than any other single bacterium. As would be expected, *escherichia coli*, aerobic streptococci, and anaerobic streptococci were also numerous.

General Clinical Signs and Symptoms

Beaver, Henthorne, and Macy (1934) noticed that whenever there was hepatic involvement by *bacteroides*, the patient had not only physical findings, but high, irregular type of fever with marked morning remissions and high afternoon exacerbations. Their cases of hepatic involvement had chills as well as systemic evidence of severe toxicity and terminal jaundice.

On the other hand, McVay and Sprunt (1952) made the clinical observation that in the majority of their cases of *bacteroides* gastrointestinal infections with liver involvement, the patients did not appear as ill as the seriousness of the infection warranted. Frequently patients had high elevation of temperature (106 degrees F) with a marked leucocytosis, yet with minimal symptoms.

Also discussing *bacteroides* infections with hepatic lesions, Hewitt in Meakins' textbook (1956) stated that jaundice plus abnormal flocculation reactions may occur. If the disease was of long-standing duration, alterations in the serum proteins and bromsulfalein retention occurred. On the whole, however, the clinical signs and symptoms of *bacteroides* infections of the gastrointestinal tract are varied, with no pathognomonic features. While it is true that some patients have a high spiking fever and appear very septic, many cases are probably overlooked because of their mild, evanescent nature. Undoubtedly, many unrecognized cases with or without bacteremia resolve themselves without treatment.

Diagnoses

At present, the frequency of diagnosis of *bacteroides* infections depends upon the degree of suspicion of the investigator. As noted, there are no clear-cut signs or symptoms. Patients are frequently more seriously ill than their clinical symptoms manifest. Basic rules for physicans to follow would include: 1. suspect *bacteroides* in liver abscesses, abscesses associated with neoplasms of the gastrointestinal tract, and in peritonitis; (frequently the pus has a putrid, foul odor); 2. look for *bacteroides* in infections of undetermined etiology which do not respond to ordinary therapy; 3. when smears show gram-negative organisms and cultures fail to grow, consider *bacteroides*. In the end, the final positive diagnosis can be made only after the bacilli have been cultured and isolated by anaerobic technics.

Treatment

Rubin et al found aureomycin to be the drug of choice in treating *bacteroides* infections. McVay and Sprunt (1952) concurred in the use of aureomycin after having also tried streptomycin, sulfadiazine, and penicillin. In their research, Fischer and McKusick (1953) listed aureomycin and terramycin as the effective therapeutic agents.

A study in 1955 by Garrod indicates that penicillin equals or exceeds other antibiotics in treatment of *bacteroides funduliformis* infections. On the other hand, *bacteroides fragilis* is resistant to penicillin and most sensitive to oxytetracycline. Garrod demonstrated all species of *bacteroides* to be relatively resistant to streptomycin and moderately sensitive to chloramphenicol.

Gillespie and Guy (1956) bring out one important fact in their studies—prolonged treatment with antibiotics is indicated. In addition, surgical drainage may be life-saving, as may be fluid balance and blood transfusions.

Summary and Conclusions

This paper has tried to point out the role of *bacteroides* in major pathological conditions associated with gastroenterology. In the gastrointestinal tract, *bacteroides* is probably a saprophyte. Under adverse circumstances, these organisms may lead to bacteremia and septicemia. In association with cancer of the colon, *bacteroides* may contribute to a rapid, downhill course. As has been noted, *bacteroides* is probably the predominant organism of the gastrointestinal tract. Therefore, it is not surprising to find it in many cases of peritonitis following perforation of the bowel. When confronted with a liver abscess, it is important to distinguish the *bacteroides* abscesses from the amebic abscesses, actinomycotic abscesses, and abscesses due to other pyogenic microorganisms, particularly staphylococci and streptococci. Nonspecific ulcerative colitis has been associated with many bacteria including *bacteroides*. Studies in the literature tend to substantiate the fact that *bacteroides* may be a pathogen even within the colon. Lastly, the importance of *bacteroides* in surgical infections is reported.

Clinical signs and symptoms of *bacteroides* infections vary greatly with the severity of the infection and the organ involved. Thus diagnosis depends a great deal on the degree of suspicion and the extent of knowledge of the investigator.

Antibiotics have been discussed, with aureomycin emerging as the drug of choice. In addition to antibiotic therapy, basic factors in treatment such as surgical drainage, fluid balance, and blood transfusions should not be overlooked.

To summarize, *bacteroides* should be considered in all infections of undetermined etiology that do not respond to routine measures. Greater awareness of the bacteriologist and physician, as well as improved laboratory facilities, should lead to increasing recognition of the significance of *bacteroides*.

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NARROWING OF PYLORUS–BENIGN OR MALIGNANT?

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The x-ray demonstration of a persistent narrowing of the pyloric area frequently presents a difficult diagnostic problem. Such lesions may be benign such as hypertrophied pyloric muscle, nonspecific benign pyloric stenosis, antral spasm due to a gastric or duodenal ulcer, spasm or fibrosis of a channel ulcer, corrosive gastritis, syphilis, tuberculosis, extraneous pressure from adjacent organs or fibrous bands, or malignant, due to infiltrating carcinoma, or lymphoma.

Probably the most common benign lesions causing narrowing of the pylorus are duodenal or gastric ulcers. It is not always possible to differentiate narrowing due to spasm and edema from scarring caused by an active ulcer, although usually the symptoms of an active ulcer may be present if the narrowing is due to a reflex spasm. If on x-ray the pylorus shows an irregularity of its contour, an eccentricity of position or a marked thinning of the barium stream, an organic lesion is usually considered. A pyloric ulcer may additionally show a crater in the pyloric canal. A duodenal ulcer, however, rarely produces a deformity in the pyloric canal unless there is an associated antral gastritis. It may however cause an eccentric position of the pylorus. On the other hand, the pyloric canal frequently cannot be demonstrated on x-ray in actual obstructions whether due to either spasm or organic stenosis. If the inability to visualize the pylorus is due to simple spasm, repeated examinations will eventually show a filling of this part.

The size of the stomach or the amount of gastric retention may sometimes be a useful sign in the differential diagnosis since there is some relationship between the duration of the obstruction and the size of the stomach.

The largest stomachs are produced by a slowly developing pyloric stenosis from peptic ulcer of the duodenum. A malignant pyloric lesion, on the other hand, infrequently permits the stomach to dilate to enormous proportions. Occasionally, however, a slowly growing scirrhous carcinoma of the pylorus may cause a tremendous dilatation of the stomach.

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Gastric analysis may be useful in differentiating the basis of a narrow pylorus. Thus histamine resistant achlorhydria in association with marked gastric retention suggests malignant disease. A high incidence of hyperchlorhydrias is found in cases of pyloric stenosis due to peptic ulcer.

Hypertrophy of the circular muscle of the pylorus in adults is often associated with prominent pyloric mucosal folds. Varying degrees of obstruction and dilatation of the stomach may be present. The condition may be the result of low grade congenital pyloric stenosis, but may also be due to pylorospasm occurring during the period of gastric ulcer activity[1]. True pyloric muscle hypertrophy in adults, without other disease in the vicinity, may be the result of a deranged autonomic nervous system; overacting vagus may induce irritability of the pyloric muscle[2]. Symptoms of hypertrophied pylorus usually start in the middle

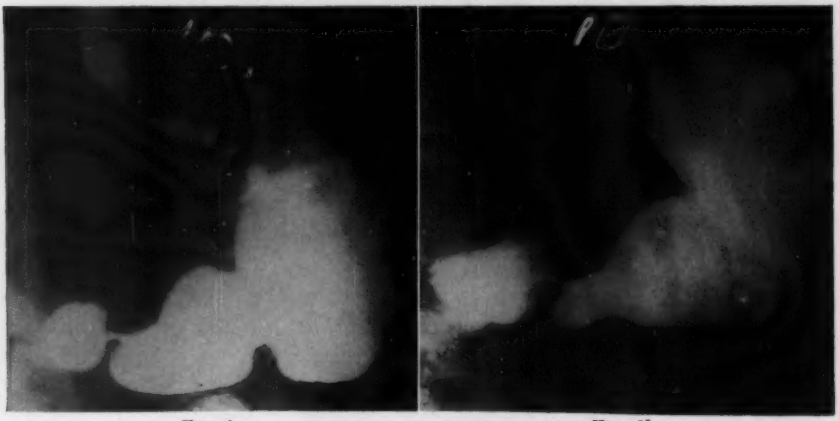


Fig. 1a Fig. 1b

Figs. 1a and 1b—Serialgrams showing findings before the first operation (1a) and before the second operation (1b). Narrowed segment longer and narrower.

or later life. There may be an ulcer-like history or only smptoms of pyloric obstruction. The pyloric canal appears smooth and very narrow on x-ray. The concavity of the base of the duodenal cap is due to pressure of the markedly thickened pylorus[3]. The latter in the absence of actual irregularity in the pylorus and adjacent antrum is suggestive of pyloric muscle hypertrophy.

Gastric syphilis may produce a narrow pylorus. The defect is often symmetrical and smooth.

Nonspecific benign pyloric stenosis is an entity that is not well defined but which is considered to be due to an inflammatory cause involving the submucosa, muscularis, and even serosa either singly or in combination. Whether this disease is a form of localized gastritis, or due to some allergic phenomenon such as the Loeffler granuloma, is still a question.

Corrosive gastritis may occasionally produce an elongated, smooth narrowing of the pylorus, associated with more or less dilatation of the stomach. This is usually a late sequel of an ingestion of a corrosive acid substance. A history of accidental or intentional acid intake will confirm the diagnosis in such cases.

Tuberculosis and lymphoma may also rarely be the cause of a persistent narrowing of the pylorus. The correct diagnosis in these instances usually comes as a surprise during the histologic examination.

Adhesions and perigastric structures may produce symmetrical defects by traction or pressure on the pylorus causing the appearance of an elongated pylorus on the roentgenogram.

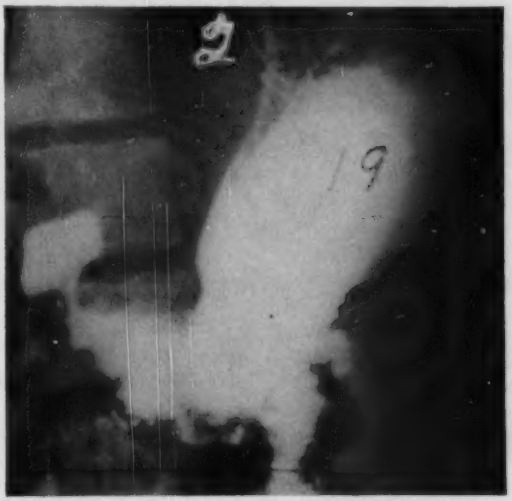


Fig. 2—Roentgenogram of an elongated pylorus which histologically proved to be syphilis.

A scirrhous carcinoma limited to the pylorus will produce an annular narrowing defect. On the films the border of the constriction may be smooth and regular in outline. About 20 per cent of all gastric cancers manifest the clinical, x-ray and pathological characteristics of pyloric stenosis. The possibility of pyloric or antral malignant disease causing the narrowing is greater if the duodenal cap is normal.

The following case reports are examples of patients encountered in our experience with this lesion and illustrate the various conditions described above.

Case 1:—H. C., a 57-year old, white male, stated that he has had epigastric distress, regurgitation, and occasional vomiting intermittently for over one year. A diagnosis of hiatal hernia was made and he was operated for it four months prior. Following the operation he did not improve but continued to have the

same symptoms plus anorexia, nausea, belching, and epigastric fullness. There had also been some weight loss.

Physical examination revealed a well developed, white, male with subicteric sclerae and a recent scar in the left upper abdomen. There were no glands or masses palpable; the liver was not enlarged. There was no succusion splash, ascites, or edema.

The essential finding on the laboratory work-up was a peculiar napkin ring contraction at the pylorus (Fig. 1a). The surgeon who had operated on the patient four months previously, informed us that the original x-rays did show a similar napkin ring deformity. He had explored the pylorus during the laparotomy, found that it was pliable and smooth, and that it easily permitted a finger through the opening. He therefore considered the pyloric narrowing on x-ray to be due to spasm and only repaired the diaphragmatic hernia.

Subsequently, we placed the patient on a bland diet and large doses of antispasmodics (1 mg. atropine, q. 6 hrs.) for a medical trial.

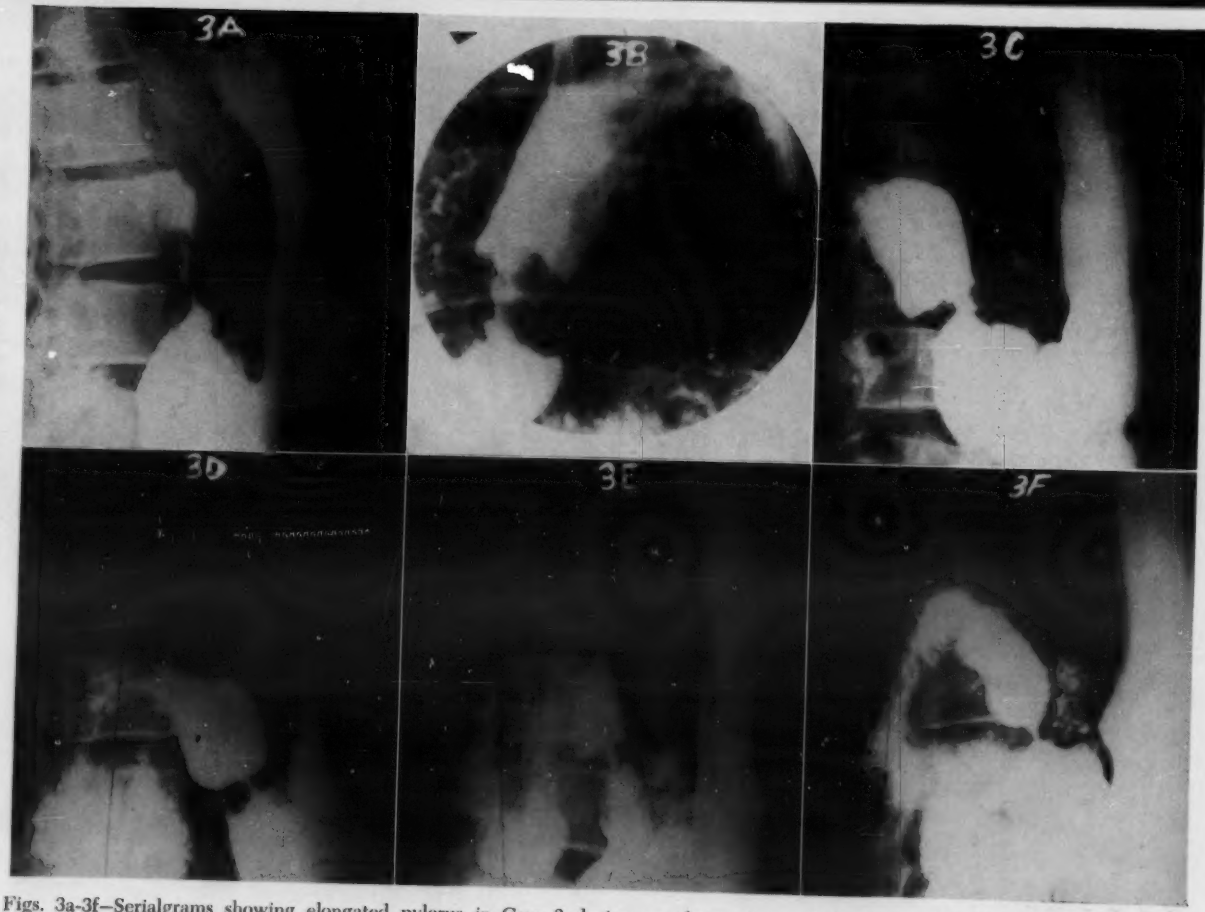
The patient had little symptomatic relief and a second x-ray series revealed essentially the same finding of a narrow pylorus (Fig. 1b). The patient was therefore advised to have surgery. He was re-operated six months after the first operation and a subtotal gastrectomy was done. Histologic examination of the resected specimen revealed an infiltrating carcinoma of the pyloric antrum.

Case 2:—W. B., a 30-year old, colored male, was admitted to the hospital because of epigastric fullness, burning, nausea, and vomiting, after meals for the past year. He also had anorexia, and lost 15 pounds during the year. Greasy foods aggravated while alkali and vomiting relieved the symptoms. He had no jaundice, melena or hematemesis. He drank moderately.

Physical examination revealed a poorly nourished, colored male, whose essential findings were tenderness in the epigastrium. The work-up revealed a positive serology and trace of albumin in the urine. X-ray of the stomach showed a narrow antrum which was considered suggestive of a carcinoma (Fig. 2).

Gastroscopic examination revealed a cobblestone appearance of the mucosa in the antrum with a superficial irregular ulcer, with poorly demarcated margins on the angulus. This picture, too, suggested to the gastroscopist the possibility of a malignancy and the patient was advised to have surgery.

At operation, an ulcer in the prepyloric region was diagnosed. The resected portion of the stomach revealed an edematous mucosa with dark purplish-red erosions and in the pyloric area a shallow ulcer, measuring 3 x 3 cm., with poorly demarcated edges. Microscopically, the section of the superficial ulcer in the region of the pylorus revealed a fairly dense fibrous connective tissue containing numerous blood vessels and capillaries. In many places, particularly about the capillaries and smaller vessels, there were large perivascular infiltra-



Figs. 3a-3f—Serialgrams showing elongated pylorus in Case 3 during an observation period of over three years. Patient has no symptoms at present. Interval between each of roentgenograms from 3b to 3f is approximately 6 to 8 months. Last roentgenogram (3f) was taken July, 1957.

tions composed of many lymphocytes, few plasma cells and large mononuclear cells. In places the capillaries showed a hypertrophy and hyperplasia of the endothelial cells. In one area, a single nerve fiber surrounded by large numbers of round cells was seen. The muscle fibers were intact. The interstitial tissue, in places, contained lymphocytes and occasional polymorphonuclear cells. About the Meissner and Auerbach plexuses, there were large accumulations of mononuclear cells. This picture was considered compatible with a diagnosis of syphilis of the stomach.

With the help of syphilis therapy, the patient made an uneventful recovery. In this patient, only the microscopic examination provided the correct diagnosis.

Case 3:—E. G., a 43-year old, white female, came to the office because of intermittent epigastric distress, fullness, belching, and nausea for several weeks and recent onset of substernal pain on swallowing. This was associated with anorexia and and some weight loss. There was no history of melena, hematemesis, constipation, or diarrhea. Her mother had died of a jaundice due to cancer.

Physical examination revealed a presence of weight loss. There were no glands palpable. The abdomen was rounded and there was marked tenderness and some resistance in the epigastrium especially to the right of the midline.

Laboratory work-up was noncontributory. The barium meal revealed a markedly elongated and narrow pylorus with retention after four hours (Fig. 3a). The patient refused surgery so she was treated with bland diet, antacids, and large doses of antispasmodics.

A repeat barium meal 10 days later showed an essentially similar picture (Fig. 3b), but because the patient felt quite improved subjectively she decided to continue the medical treatment. She has remained under medical supervision for the past four years, has gained weight, and feels quite well. Repeat x-ray studies of her stomach during the past three years have shown improvement, but persistent narrowing of the pylorus (Figs. 3c, d, e, f and g).

Case 4:—H. G., a 57-year old, white male, was first seen because of epigastric distress, especially after fatty foods, cramp-like abdominal pain, nausea and intermittent vomiting of three months' duration. These symptoms which at first responded to a medical treatment have recently become considerably worse. There was no previous history of similar symptoms or of melena or hematemesis. His bowel movements were usually normal.

Physical examination revealed a stocky, male, with an emphysematous chest and a marked obese abdomen which made abdominal palpation very difficult. There was, however, definite tenderness in the epigastrium. There was no ascites or edema.

Laboratory work-up was not significant except for a fasting blood sugar of 162 mg. per cent. X-ray studies revealed a marked narrowing of the pylorus

Figs. 4a-4f—Serialgrams of Case 4 showing little changes during 3½ years of observation in this patient. No clinical symptoms at present, while on an ulcer regimen. Interval between each of the roentgenograms is approximately 6 months. Last roentgenogram was taken July, 1957.

(Fig. 4a), and a poorly contracting large gallbladder. Because the patient refused surgery, he was placed on a strict ulcer regimen of diet, antacids and large doses of antispasmodics. A repeat stomach x-ray four weeks later showed some improvement as compared with the previous films.

He has been treated medically for the past three and a ha[illegible]ears and there has been some improvement in his x-ray findings (Figs. 4b, c, d, e, f and g). Subjectively he has felt well and returns every 3-4 months only for a general check-up.

Case 5:—M. S., 40 year old, white female, was admitted into hospital because of intermittent epigastric pain, vomiting, weakness and fatigue for five

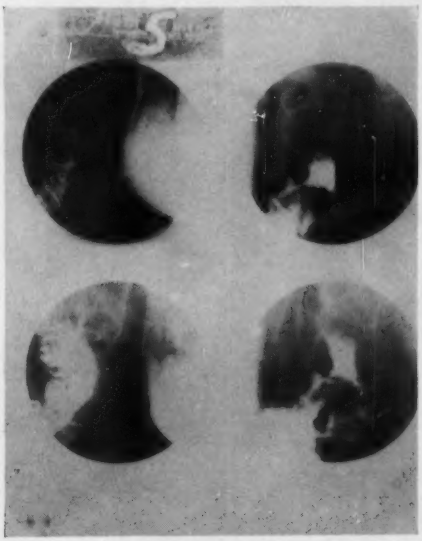


Fig. 5—Roentgenogram of narrowed pylorus which on histologic examination revealed a hypertrophic pyloric muscle and a healed gastric ulcer.

months. The pain started ten minutes after eating and was not relieved by food or alkali. She had several bouts of black stools and lost 30 pounds in five months.

She had an appendectomy at the age of 12, and a cholecystectomy at 17.

Physical examination revealed mainly a very tender cystic mass, the size of a small orange, in the right upper quadrant which moved with respiration, and was not believed to be the liver.

Laboratory work-up was noncontributory. X-rays of the upper gastrointestinal tract revealed a narrowing of the antrum and pylorus which was suggestive of a malignant lesion (Fig. 5).

The patient was operated upon and a subtotal gastrectomy was performed.

The resected portion of the stomach revealed a 2 mm. firm scar with radiating stellate mucosal folds at the angulus, while at the pylorus there was a diffuse palpable thickening. Section taken longitudinally, through the pyloric ring revealed preservation of mucosa and a moderately edematous and vascular submucosa. The ganglion cells of Auerbach's plexus were present and nerve bundles in the wall were apparently somewhat increased and thickened. The findings were considered compatible with a hypertrophy of the pyloric muscle and a healed gastric ulcer.

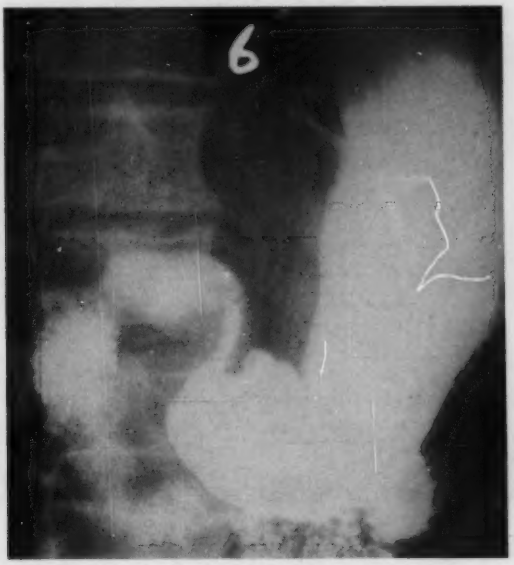


Fig. 6—Roentgenogram of an elongated narrow pylorus which on operation was ascribed to adhesions.

Case 6:—J. M., 71-year old, white male, entered the hospital with a history of anorexia, weight loss, epigastric distress worse on eating and constipation for several months.

On physical examination the essential findings were marked emaciation and inability to walk. The liver and spleen were not palpable; there was no ascites or edema. The laboratory work-up was negative except for slight anemia. Gastrointestinal x-ray showed marked narrowing of the antrum with a suggestive niche along the lesser curvature (Fig. 6).

Because of the above findings and poor response to treatment, operation was suggested. At operation the surgeon found adhesions extending from the

porta hepatica to the pylorus and antrum causing a tenting of the lesser curvature and narrowing of pylorus. A gastrotomy in the antrum was performed, through which the pylorus and antral mucosa were examined and determined to be normal by "feel" and "look". The surgeon, therefore, closed the gastrotomy and finished the operation as an exploratory, satisfied that the x-ray findings could be explained on the mechanical basis as described above.

Case 7:—L. B., 62-year old, male, entered the hospital because of steady upper abdominal pain, nausea, belching and vomiting of two weeks' duration.

On physical examination, patient appeared dehydrated and quite ill. There was a baseball-sized mass in the upper right quadrant, nontender, nonmovable, firm and separate from the liver.

Results of laboratory examinations were not significant.

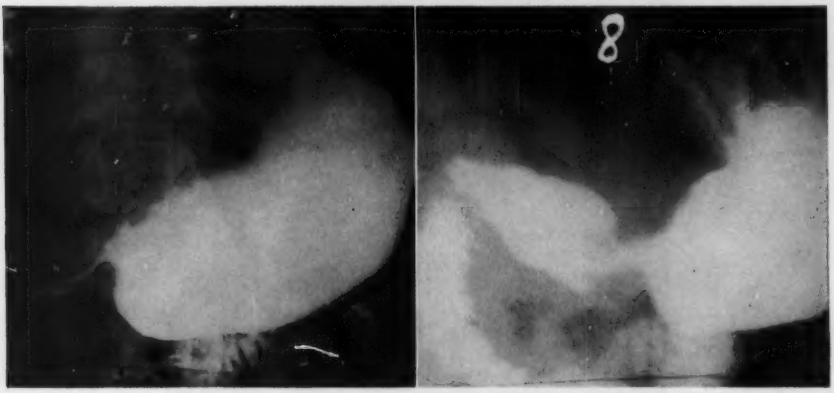


Fig. 7 Fig. 8

Fig. 7—Roentgenogram of elongated narrow pylorus which on operation was ascribed to adhesions.

Fig. 8—Roentgenogram of an elongated narrow pylorus which on operation was considered secondary to a previous antral ulcer.

X-ray of the stomach revealed narrowing of the pyloric antrum compatible with a carcinoma (Fig. 7).

At operation, the pylorus and antrum were apparently normal, but were anatomically dislocated by firm adhesions to the gallbladder. These were separated and a biopsy of the gallbladder wall was taken. Microscopically the latter revealed severe chronic inflammatory reaction.

Case 8:—H. C., 60-year old, white male, complained of abdominal distress, nausea, anorexia, weight loss, and intermittent vomiting of several months' duration. Several years ago he had been told that he had an ulcer, the site of which he didn't know.

Physical examination revealed a well developed, well nourished, man whose essential findings were tenderness in the right epigastrium. There were no masses felt.

Laboratory findings were essentially normal. X-rays of the stomach, however, revealed a constricting prepyloric lesion, with stiffness of the walls, suggesting a carcinoma (Fig. 8). Surgery was advised, but the patient refused. Because of aggravation of symptoms and more frequent bouts of vomiting, during the ensuing several months, he finally consented to surgery.

At operation, the pyloric area was markedly narrowed and firm. Subtotal gastrectomy was done. Microscopically, section of this area revealed scar tissue, probably from a previous benign ulcer.

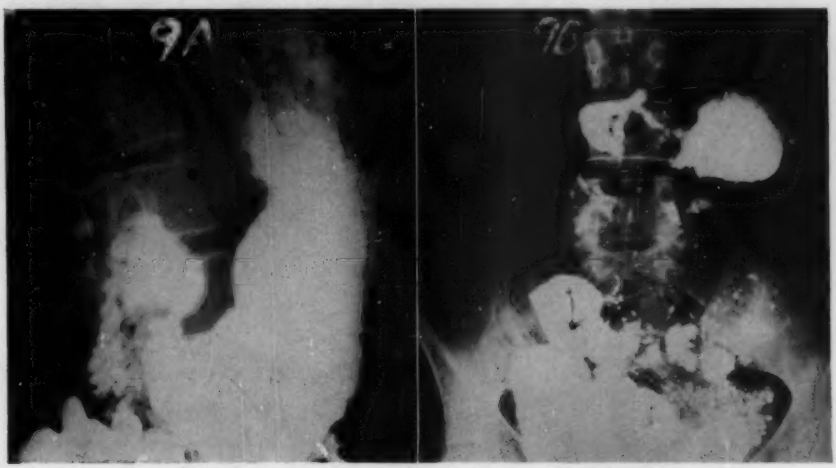


Fig. 9a Fig. 9b

Figs. 9a and 9b—Serialgrams of an elongated pylorus during the barium meal examination (9a) and 3 hours afterwards (9b). Histologically the lesion was benign, possibly due to an ulcer.

Case 9:—N. B., 52-year old, female, was admitted to the hospital because of epigastric pain radiating to the back, headaches, anorexia, nausea, belching, and intermittent vomiting. Four years prior she had been told that she had a narrowing in her stomach and should be operated. She, however, refused surgery and continued on diet and medications which relieved the symptoms intermittently. During the past few months, however, the symptoms became worse, so that she consented to surgery. She had previously had operations for gallbladder, appendicitis, and for pelvic pathology.

Physical examination revealed essentially an underweight woman showing signs of weight loss. There were three surgical scars on the abdomen, but no masses, liver or spleen were palpable.

Except for a slight anemia, the laboratory work-up was not significant, (Fig. 9a). X-ray examination revealed a marked narrowing of the pyloric area which was persistent and which was associated with a 50 per cent retention of barium after three hours (Fig. 9b).

At operation the antrum appeared very rigid, but nothing else was found. A subtotal resection was done. Microscopically, the resected area revealed scarring as from an old ulcer.

Case 10:—N. B., a 58-year old man was seen because of epigastric distress and nausea with intermittent vomiting of several months' duration. Prior to this he had anorexia and weight loss. The patient stated that he has had a peptic

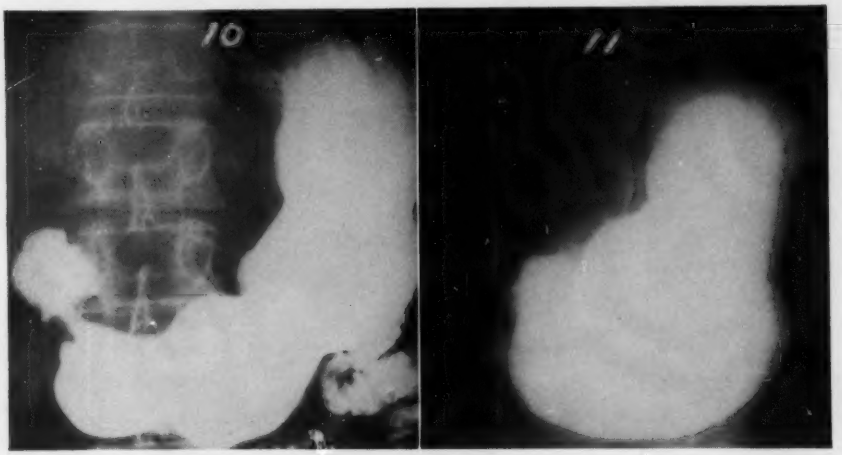


Fig. 10 Fig. 11

Fig. 10—Roentgenogram of a narrowed pylorus which was found to be due to an infiltrating carcinoma.

Fig. 11—Roentgenogram of a narrowed pylorus which was considered to be a sequela of corrosive gastritis.

ulcer for many years for which he took treatment very irregularly but nevertheless felt moderately well until onset of present symptoms. He smoked moderately but had stopped the use of alcohol.

On physical examination the essential findings consisted of a slight, undernourished elderly man, not acutely ill, but complaining of abdominal cramp-like pain. Examination of chest and abdomen failed to reveal any abnormal findings.

The results of the clinical laboratory examination were noncontributory. The roentgenograms of the stomach showed a narrowing of the pylorus and a scarred duodenal bulb (Fig. 10).

Gastroscopy revealed a stiff, immobile antrum which was diagnosed as infiltrating antral malignancy and an operation was advised.

At operation, the surgeon could not feel any infiltration in the pyloric area, neither from the outside nor through a gastrotomy. Because he felt no constricting lesion and his finger passed readily through the pylorus, he terminated the operation without other procedures.

The patient made an uneventful recovery and left the hospital, but continued to have the same symptoms despite diet and medication. About six months later he therefore entered another hospital where a subtotal resection of the stomach was done. Microscopically, the pyloric region revealed an infiltrating scirrhous carcinoma.

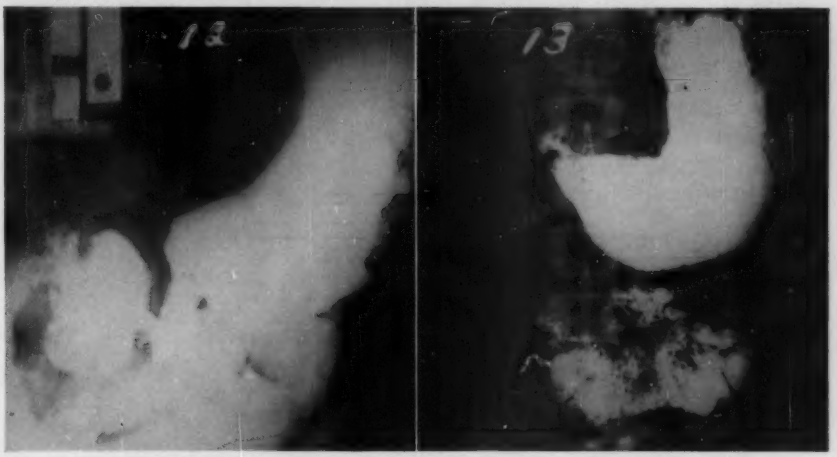


Fig. 12 Fig. 13

Fig. 12—Roentgenogram of an elongated pylorus which was found histologically to be due to a Hodgkin's granuloma.

Fig. 13—Slightly elongated and persistent narrowing of pylorus with marked gastric retention in a patient with intermittent porphyria.

Case 11:—G. H., a 58-year old maintenance man was seen because of increasing weakness, weight loss, anorexia, epigastric fullness and constipation which seemed to have developed insidiously. There was no history of previous gastrointestinal disorders. A significant factor in the past history was the accidental drinking of a small amount of "muriatic acid" several months prior. Except for an initial burning in mouth and throat, this accident had, in his opinion, no other untoward results.

On physical examination he showed signs of weight loss, but was not otherwise ill. There was some fullness in the epigastrium and a succussion splash was heard.

Laboratory work-up gave mostly equivocal results. X-ray of the stomach showed a very large stomach with an eccentrically situated elongated pylorus and a normal appearing duodenal bulb (Fig. 11). A carcinoma of the pylorus was considered. At operation the antrum appeared much thickened and the pylorus particularly was firm, and surrounded by many adhesions. Because of the history of acid ingestion, the diagnosis of corrosive gastritis was considered. Because of the patient's age, however, resection was performed. The histologic examination revealed only changes of chronic inflammation.

Case 12:—M. G., 54-year old, male, entered the hospital because of pains in the epigastric area associated with fullness, belching, and anorexia. He had lost weight and had intermittent vomiting shortly before entering the hospital.

Physical examination revealed a somewhat pale patient, not acutely ill. The essential findings were tenderness in the epigastrium and suggestive resistance. The abdomen was slightly distended.

Laboratory work-up was not significant except for a slight anemia. X-ray of the stomach revealed mainly a slightly elongated, persistent narrowing of the pylorus (Fig. 12). The patient was diagnosed as a carcinoma of the stomach and surgery was performed.

Histologic examination of the resected specimen and of some perigastric glands revealed Hodgkin's granuloma.

Comment

Our aim in this paper is to stress the importance and dangers of a narrow pylorus and not to describe a new syndrome. Accordingly, we have not presented the clinical histories of some of the representative cases in great detail. The entire subject was reviewed by Dr. H. A. Bockus and his associates some years ago in one of the gastroenterology postgraduate courses and subsequently published[4]. Since then many problems relating to the narrow pylorus have frequently puzzled us and prompted us to again report some supposedly well known, but often neglected facts.

The roentgen defect of a narrow pylorus must be considered as a dangerous organic lesion until proven otherwise. The definitive diagnosis can be made only by careful multiple histological examination of the specimen.

Clinically the enigma of a narrowed pylorus still rests on the question of whether it is benign or malignant, since they may closely resemble each other in many aspects.

The duration of the illness, weight fluctuations, vomiting and degree of gastric acidity are not of diagnostic value. Thus among our cases, the patient with a history of illness of a few weeks' duration had an apparently benign lesion while two patients, one with a history of abdominal distress of over one year and

another with a history of ulcer distress of several years' duration had malignant lesions. Similarly, weight loss was found to be as great in some of the patients with benign as with malignant lesions. Vomiting was also noted intermittently in most of the patients, although actual demonstrable gastric retention was found only in three patients in our group. The fact that a patient feels improved and the lesion does not worsen in time, does not definitely rule out a malignancy. Indeed we are uneasy about the two unoperated patients reported here, for one cannot be sure that the lesions are benign, despite the prolonged course. Bockus[4] presented a patient, in whom a narrow pylorus lesion, for which a gastroenterostomy was done, had progressed from a short narrowing, similar to that seen in our patients, to a smooth markedly elongated narrowing, in a period of six years. Repeat surgery finally proved it to be a submucosal carcinoma of the antrum associated with a marked pyloric muscle hypertrophy. It is because of such experiences that one cannot tell definitely the nature of the lesion in our two unoperated patients.

From the x-ray findings, one must conclude that the lesions present in the photographs of our cases are organic. Regional spasm is unlikely when the lesion is of long duration and persistent. The presence of an ulcer might indicate that pyloric narrowing is secondary to it, either as spasm or hypertrophy of the pylorus muscle. This may be a dangerous assumption for actually, there is no way of differentiating by x-ray, a benign from a malignant lesion. At times, the question arises whether hypertrophic rugae might be the cause of a pyloric narrowing. We have recently reviewed a series of cases of hypertrophied rugae, but in none was a narrow pylorus a diagnostic problem, either radiologically or gastroscopically[5].

The more common causes of narrow pylorus are first, stenosis resulting from a peptic ulcer, second, a hypertrophied pyloric muscle similar to that found in children, which are being more frequently reported and third, infiltrating carcinoma. Other causes are syphilis, corrosive gastritis, Hodgkin's disease, tuberculosis and nonspecific benign pyloric stenosis. Extrinsic factors, such as adhesions may, by distortion, create the picture of a narrow pylorus, but even here surgery is indicated for diagnosis and incidentally to prevent or relieve obstruction. The surgical and histological reports of our cases illustrate practically all of the mentioned diseases with the exception of tuberculosis. Our two nonoperated patients might be classified in the category of nonspecific benign pyloric stenosis.

Apropos to the observations by Horton[2] that a deranged autonomic nervous system may be the cause of a pyloric muscle hypertrophy, we wish to mention our experience with a patient in whom persistent pyloric narrowing (Fig. 13) caused obstruction and led to a surgical exploration. At operation nothing was found and postoperatively the patient developed a multitude of symptoms which led to the diagnosis of intermittent porphyria, proven by a positive test for porphobilinogen.

Despite the well known fact that it is impossible to diagnose a gastric lesion by "look" or "feel", some surgeons still practice this method of diagnosis. Often at gastric surgery, when a narrow pylorus is found, the surgeon will not perform the previously agreed upon resection or biopsy, because the pylorus is not rigid or permits the finger to go through the pylorus. Since in some of our cases the surgeon relied on the "feel" of the lesions to make a definite diagnosis of a benign lesion, one must repeat Dr. Bockus' statement that a submucosal malignant lesion actually may not be recognized by "feel" or "look" as readily as a hypertrophied pyloric muscle. The surgeon must remember that with a patient under deep anesthesia, the tissues may feel softer than they normally would under natural conditions. Hence, if at operation, the surgeon cannot feel the narrowing of the pylorus which is so obvious on the x-ray, he should become even more suspicious of a malignant lesion.

Biopsy of the narrowed pylorus may occasionally give us additional information. In the two of our cases in whom the narrowing was ascribed by the surgeons to be due to adhesions, one must also consider the additional presence of a hypertrophied pyloric muscle as was found in the patient reported by J. E. Berk[4]. In Berk's case the surgeon found adhesions extending from the lesser curvature of the antrum to the liver and decided that the pyloric deformity present on x-ray was produced by the downward drag of the barium filled stomach. A biopsy of the pyloric region, however, revealed changes compatible with chronic gastritis and hypertrophy and thickening of the pylorus.

While the biopsy in Dr. Berk's case revealed an additional cause for the narrowing, it must be stressed that a negative biopsy does not always rule out a malignancy.

In this type of lesion it is almost as dangerous to rely on the results of a biopsy for definitive diagnosis of a malignancy as in cases of perisigmoiditis or diverticulitis with tumor formation. The finding of cancer cells is positive proof for a malignancy, but a negative biopsy is not definitive. In many so-called chronic inflammatory lesions, perseverance in examining many histologic sections may result in the finding of malignant cells.

Just as the biopsy is not always a helpful diagnostic measure, none of the other presently used diagnostic procedures are of much value. Thus the amount of free acid, the absence of cancer cells in the gastric sediment or findings on gastroscopic examination cannot aid much in the accurate diagnosis of a pyloric narrowing. The only reliable procedure is resection and careful histological examination of the resected specimen.

Conclusions

1. The finding of a narrow pylorus on x-ray examination signifies a dangerous lesion.

2. There are no diagnostic criteria which can replace painstaking histologic examination of many slides of the resected specimen.

3. A simple biopsy is not sufficient for a definitive diagnosis.

4. Resection is the only logical procedure for all cases of narrow pylorus, since benign lesions must also be removed in this area, for the welfare of the patient.

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INCIDENCE OF ESOPHAGEAL VARICES IN CIRRHOSIS OF THE LIVER*

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During the last decade there has been an enormous increase in the study of portal hypertension as a consequence of the new surgical technics that have brought hope in the treatment and prevention of a previously almost uniformly fatal condition: massive gastrointestinal hemorrhage from bleeding esophageal varices. The demonstration of the esophagogastric varices has been the indirect clinical method of diagnosing the existence of hypertension in the portal system.

For the past three years, the authors have been interested in the study of esophageal varices in cirrhosis of the liver and in comparing the results obtained by the esophagoscopical and radiological methods in their demonstration[1,2]. Notwithstanding recent publications in this particular field and the enormous literature on portal hypertension, we feel that there is still need for further investigation. The incidence of varices in liver cirrhosis varies in the published material, as will be seen in the following short review of the literature.

Review of the Literature

It is quite logical that the incidence of varices has been considered greater in cirrhotics with bleeding episodes. Preble's frequently quoted paper refers to 60 cirrhotics dying of gastrointestinal hemorrhage[3]. In this group, he found that 85 per cent had esophageal varices. Bockus[4] gives us a similar figure on estimating that 80 per cent of bleeding episodes in cirrhotics are due to varices. Halstead and Fainer[5] found 76.1 per cent of varices in 41 cirrhotics with 46 bleeding episodes. Palmer and Brick[6] studied 59 cirrhotics with important gastrointestinal hemorrhage and found varices in 47, or 79.6 per cent. From their own work, and the previously quoted statistics, these authors[7] have estimated that, in cirrhotics with hemorrhage, 15 to 20 per cent will not have esophageal varices as explanation for their bleeding.

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Even though there is some agreement in the estimation of varices in bleeding cirrhotics, the same is not true when we consider nonbleeders, or even those estimates in which cirrhotics have been considered as a whole, without taking into consideration their hemorrhagic tendency.

Ingelfinger[8], without citing source, has estimated that varices are present in 80 to 90 per cent of cirrhotics.

In autopsy material, Weinberg[9] found varices in 17, or 57 per cent, of 30 cases of portal cirrhosis, and in 2 of 6 cases of biliary cirrhosis. In his material, a majority of the cases were nonbleeders. Bjornboe and Raaschou[10] compared the autopsy findings in cases of subchronic atrophy of the liver and in portal cirrhosis, finding an incidence of varices in 48 of 108 cases of subchronic atrophy, or 44.8 per cent, and in 42 of 76 cases of portal cirrhosis, or 58 per cent. Autopsy material, therefore, seems to be able to demonstrate varices in approximately 50 per cent of cirrhotics.

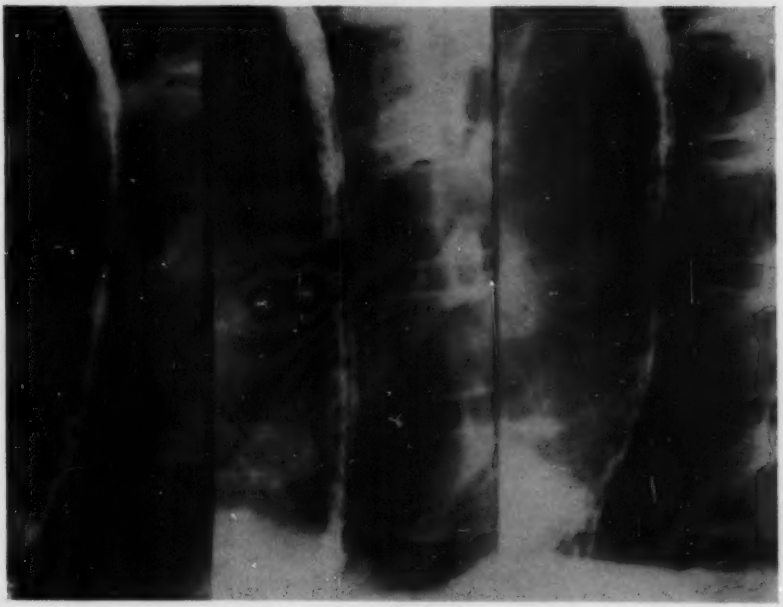

Fig. 1–Portal cirrhosis with ascites. Esophagoscopy demonstrated small varices. Radiology: irregular border and small filling defects in lower third of the esophagus.

The radiological demonstration of esophageal varices has shown a greater variation. Ever since the comparatively recent first demonstration of varices by barium swallow by Wolf[11] in 1928, a not too numerous but continuous amount

of published material has appeared. Schatzki[12] was of the opinion that varices could be demonstrated radiologically in approximately 50 per cent of cirrhotics. Templeton[13] in 1944, stated that varices could actually be demonstrated by the barium swallow in about 40 per cent of the patients that actually had them. Zaino[14] has mentioned figures that vary from 15 to 50 per cent in demonstrating proved varices by x-ray. Hare, Silveus and Rouff[15], in a group of cirrhotics with varices demonstrated postmortem in 50 per cent, found radiological evidence of varices in only 15 per cent. Brick and Palmer[7], on studying 150 cases of histologically proved cirrhotics, found that varices could be demonstrated radiologically in only 12.9 per cent. More recently, Atkinson[16] and a group of British workers

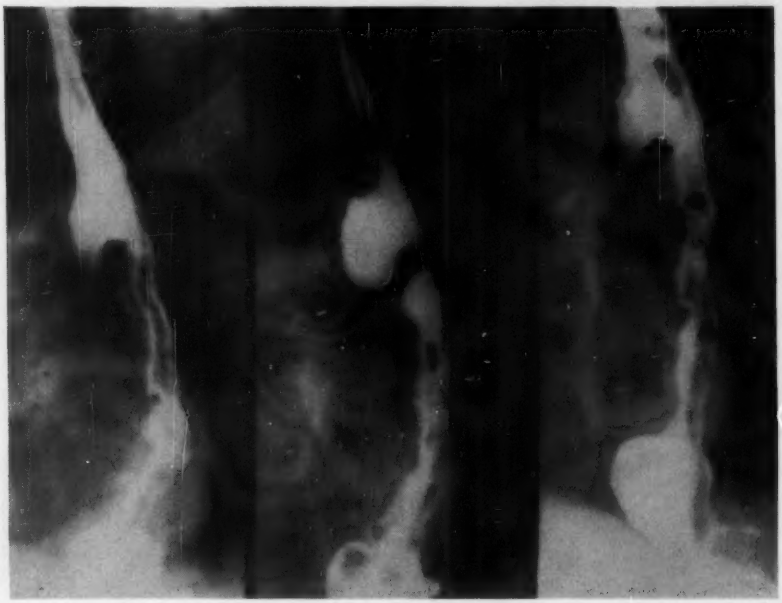

Fig. 2—Patient with portal cirrhosis. Esophagoscopy: large varices in lower third of the esophagus. Radiology: large rounded filling defects in lower and middle third of the esophagus.

in London, have found that the esophagogram demonstrated varices in 60 per cent of individuals in whom said varices could be demonstrated by portal venography. Evans[17], of New York Hospital, in an evaluation of the esophagogram as a method of study, has said that varices could be made evident by it in from 75 to 80 per cent of the cases. Nelson[18] has estimated that, even if the radiologists avail themselves of the best equipment and technics, they are at best only able to show varices in about 30-50 per cent of those patients known to have them. Lavigne[19] has been able to find varices in only 36.6 per cent of 60 cases of portal hypertension.

The esophagoscopic method of study in the demonstration of esophageal varices has almost universally been considered superior to x-ray. The method has not, however, received due consideration, possibly from fear of danger in its use. To our knowledge, the method has received extensive trial only in the hands of Palmer and Brick[7] who demonstrated varices in 95 of 150 histologically proved cirrhotics, with an incidence of 63.3 per cent varices in cirrhosis. Lavigne[19] in more recent material, demonstrates unquestionable evidence of varices in 65 per cent of 60 known cases of portal hypertension and a condi-

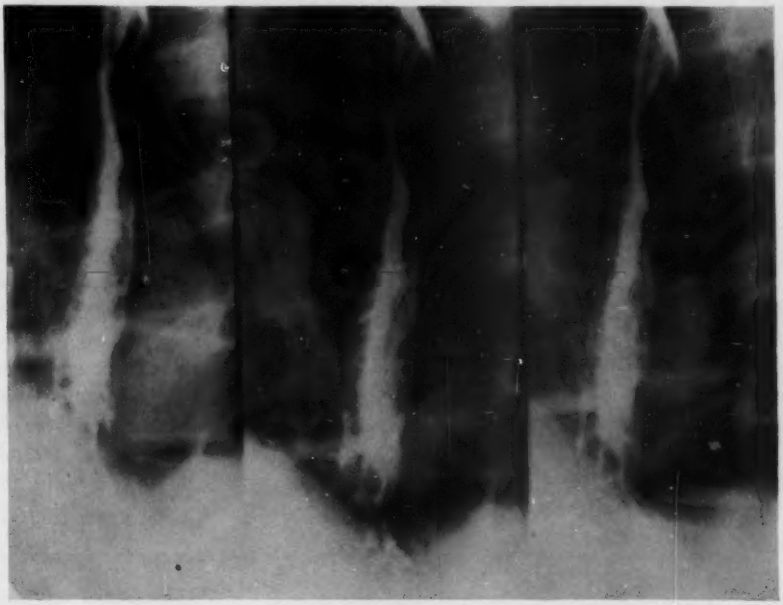

Fig. 3—Patient with portal cirrhosis. Esophagoscopy demonstrated presence of varices. Above spot-film shows round filling defects and indented borders characteristic of varices.

tion he calls prevaricose state in the remaining 35 per cent. If this prevaricose state is considered diagnostic, he has a 100 per cent incidence of varices in portal hypertension diagnosed endoscopically.

Material and Methods

With the idea of clarifying the conflicting results seen in the aforementioned publications, and following, to some extent, the method of study of Brick and Palmer[7], we planned the systematic investigations of varices in individuals in whom cirrhosis of the liver was suspected clinically and would be demonstrated, mostly by peritoneoscopy and biopsy of the liver, at times by

biopsy alone and, in a few instances, by surgical biopsy or postmortem study. The individuals were generally remitted to the endoscopical or radiological departments with the specific intention of the investigation of esophageal varices, but without information as to whether the diagnosis of varices had or had not been substantiated. This was done with the deliberate intention of checking overenthusiasm on part of the investigators. In a minority, these individuals were bleeders with the clinical diagnosis of cirrhosis, but in a large majority they were cases of compensated cirrhosis or cases of latent cirrhosis discovered accidentally during peritoneoscopy. In our hospital, peritoneoscopy has been performed almost routinely in some departments of clinical medicine for the diagnosis of obscure abdominal conditions. This has placed in our hands a large amount of cases of latent cirrhosis, without clinical manifestations, of course, and, at times, without laboratory evidence.

From this material we have chosen 62 anatomically proved cases. Those cases eliminated have been so for the only reason that, either a final diagnosis was not established or the combined esophagoscopical and radiological examinations were not performed.

This material can be divided into 39 cases of portal cirrhosis, 12 cases of postnecrotic cirrhosis, 7 cases of biliary cirrhosis and 4 cases of adenocarcinoma with cirrhosis (primary liver carcinoma with chronic cirrhotic changes). All the esophagoscopical and radiological investigations in this study were performed exclusively by the authors. Esophagoscopy (CJS) was performed with Roberts 12 x 16 x 50 and Jackson 10 x 53 esophagoscopes. We have never observed untoward effects attributable to instrumentation. Radiological technic (LBS) has been detailed in a previous communication. In no case did the authors communicate their results until both investigations were completed.

Results

From the very beginning of our study, we have been surprised by the high percentage of varices discovered in our cirrhotic cases. Esophagoscopy has diagnosed varices in 60 of 62 cases of histologically proved cirrhosis, giving an incidence of 96.7 per cent varices in cirrhosis of the liver (Table I); radiology discovered varices in 58 of the 62 cases, or 93.5 per cent. The two cases negative to esophagoscopy were also negative to radiology and the two cases positive to esophagoscopy and negative to radiology were patients with minimal endoscopic alterations corresponding to varices. Both of these patients were peritoneoscopic cases with small retracted livers. The two patients without varices in both investigations were also peritoneoscopic cases with evidence of advanced morphological cirrhosis. In one of these cases there was evidence of increased intraabdominal collateral circulation. A transhepatic portal pressure determination was 50 c.c. of water.

In no case did we make the diagnosis of varices by either method that did not have some type of portal block on subsequent investigation, even though many of the cases referred to us for study did not have cirrhosis on further investigation and were, therefore, omitted from this material. In other words, we have not encountered cases of so-called idiopathic varices of the esophagus.

Comment

In our material, varices have been present in 60 of 62 cases of histologically proved cases of cirrhosis of the liver, giving a net incidence of 96.7 per cent. Our only explanation for the results we obtain is the thoroughness and care with which each investigation was done and, probably not least, the preconceived idea that each investigation was done specifically to search for varices. Our superior results over autopsy material will not surprise those who know the ease with which these structures collapse on cessation of portal hyperten-

TABLE I

Comparison of Esophagoscopic Study and X-ray in 62 Cases of Cirrhosis

	Total	Var.	No Var.
Esophagoscopy	62	60	2
X-ray	62	58	4
Positive esophagoscopy, negative x-ray	2		
Positive x-ray, negative esophagoscopy	0		
Positive to two methods	58		
Negative to two methods	2		

sion. The extraordinary results of the radiological investigation are due to a proper and not too elaborate technic, the exclusive use of spot-film radiology and a large dose of patience. Our endoscopic results have been due to a correct interpretation of very early alterations corresponding to esophageal varices. We have the impression of having correctly interpreted as varices, many incipient cases that could previously have been classified as normal.

Our satisfaction lies in the fact that, up to the present, we have not made the mistake of diagnosing varices in a normal portal system.

Summary

We present a short review of the literature giving the incidence of esophageal varices as obtained by clinical estimates, autopsy material, esophagoscopy and radiology.

The present study consists of 62 cases of histologically proved cirrhosis in which varices were diagnosed in 60 cases by esophagoscopy. This demonstrates a net incidence of 96.7 per cent varices in cirrhosis of the liver. The radiological method demonstrated the presence of varices in 58 of the 62 cases, or an incidence of 93.5 per cent. The two cases negative to esophagoscopy were also negative to radiology.

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PYLORIC STENOSIS RESULTING FROM CORROSIVE GASTRITIS*

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Corrosive gastritis is a comparatively rare condition, but it probably occurs more frequently than appears from the few cases reported in the literature. As several observers have pointed out, the reason for the paucity of reported cases is that so few patients survive the initial acute phase of the corrosive poisoning for more than 24 hours. The small number of cases reported deal with those that develop pyloric stenosis, its characteristic late sequel.

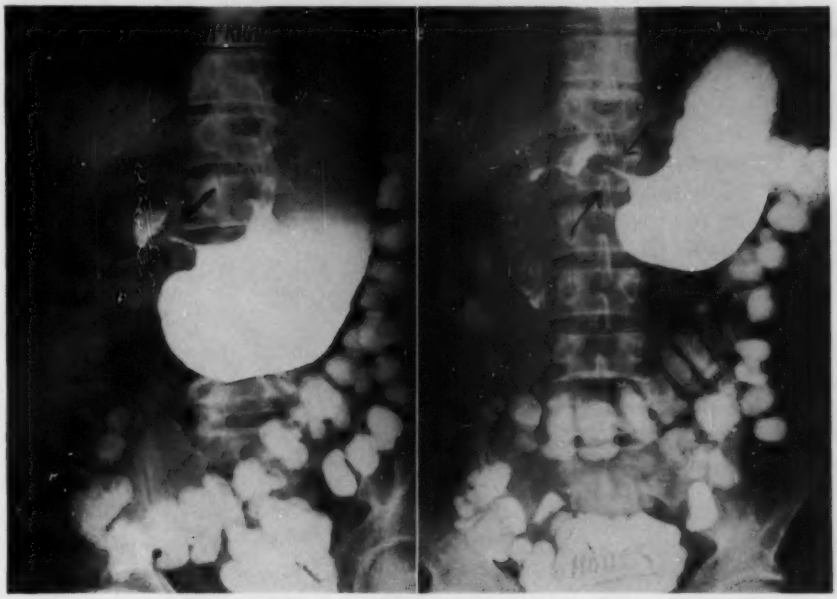

Fig. 1 Fig. 2

Fig. 1—Large atonic stomach showing hypersecretion, shortening of the lesser curvature and a smoothly outlined narrowing of the pyloric antrum producing a stricture.
Fig. 2—Six-hour film showing a 90 per cent gastric residue and pyloric antrum strutcure.

The clinical syndrome of corrosive gastritis with the subsequent development of pyloric stenosis was first described in 1828 by Robert[1], a Frenchman.

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Halstead[2], in 1917, reported the first case in this country. Crohn[3], in his book *Affections of the Stomach,* published in 1927, cited three cases.

In 1930, Boikan and Singer[4] reported five cases seen by them in 1½ years at the Cook County Hospital in Chicago. They observed that a greater number of case reports came from the European continent than from the United States and Great Britain. McLanahan[5], in 1934, and Gray and Holmes[6], in 1948, reviewed the subject and each added another case. In 1951 Karon and Wall[7] surveyed the world literature and found a total of 140 reported cases, of which only 12 were from the American literature.

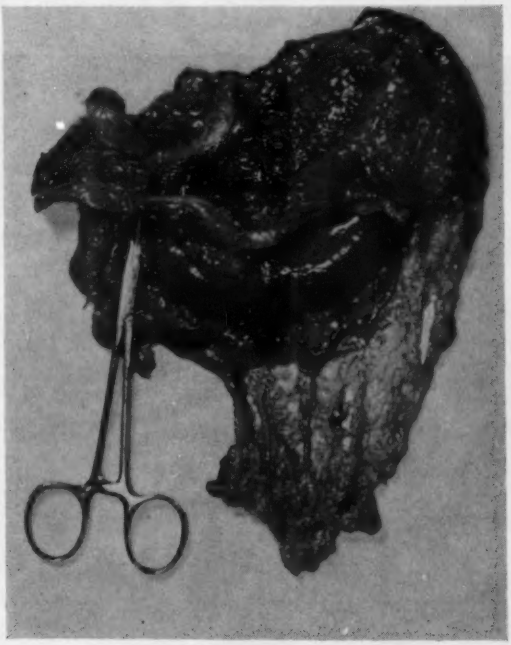

Fig. 3—Stomach opened showing thickened walls of the pyloric antrum due to extensive fibrosis.

Steigmann and Dolehide[8], in 1956, in an excellent contribution discussing the clinical, pathological, roentgenological, and therapeutic aspects of this condition, added 4 more cases. The following case is the first encountered at the Jersey City Medical Center.

Report of Case

A 33-year old laborer, depressed over personal problems and while in a drunken stupor, swallowed an unknown quantity of a commercial cleaning fluid,

later found to contain a 20 per cent solution of muriatic (hydrochloric) acid. He was admitted to the Jersey City Medical Center on 20 November 1954, about one hour after the ingestion of the corrosive. On admission, he was in acute alcoholic intoxication, incoherent, and uncooperative. The blood pressure was 140/100, pulse 90 and respirations 24. The oropharynx was free of burns and the remainder of the physical examination was essentially normal.

Treatment was supportive, consisting of gentle gastric lavage with a mild alkaline solution, sedation and parenteral fluids.

On the day after admission, the patient was mentally clearer and complained of epigastric pain and tenderness with intermittent vomiting of small quantities of coffee-ground material.

On the fourth hospital day an area of ulceration and oozing of blood was noted on the uvula and the posterior pharyngeal wall appeared reddened.

On the eighth day he suddenly vomited about 500 c.c. of bright red blood, became faint and pale, and went into shock with blood pressure of 90/60, pulse 150, temperature 104° F, and hematocrit 29 per cent. He also developed signs of bronchopneumonia. Energetic supportive treatment was given in the form of repeated plasma and blood transfusions, intravenous aureomycin and steroid therapy. He remained in critical condition for three days, after which he gradually improved, complaining only of a slight burning sensation in the throat and and mild epigastric tenderness.

On the 19th day, roentgen study of the gastrointestinal tract revealed the following: The esophagus appeared normal except for intermittent spasm at its lower end, with slight delay in the passage of barium, but no evidence of stricture. The stomach appeared normal except for some narrowing of the lumen of the pyloric antrum, believed to be due mainly to spasm. The remainder of the gastrointestinal tract showed no abnormalities.

On the 25th day esophagoscopy revealed a reddened epiglottis with slight excoriation, a few superficial ulcerations in the upper third and lower end of the esophagus, and no evidence of stricture.

The patient continued to improve rapidly. Roentgen re-examination of the esophagus showed it to be apparently normal. He was discharged on the 45th hospital day and advised to return if he developed any symptoms.

On 4 February 1955, (12 days after discharge and 8 weeks after the inital episode) he was readmitted to the hospital because of inability to retain either liquids or solid food, weakness, and a weight loss of 20 pounds. Esophagoscopy showed no stricture in the esophagus. Roentgen study of the upper gastrointestinal tract revealed a normal esophagus, a rather large atonic stomach with hypersecretion, shortening of the lesser curvature, a smoothly outlined narrow-

ing of the pyloric antrum producing a definite stricture (Fig. 1), and a 90 per cent gastric residue at six hours (Fig. 2). Although the filling defect strongly simulated that of carcinoma of the pyloric antrum, knowledge of the history happily helped in arriving at the diagnosis of pylorus stenosis due to fibrosis following corrosive gastritis.

A subtotal gastrectomy was performed. The specimen revealed a fibrous tumor, 2.5 x 6 cm., completely occluding the pylorus, with marked thickening and shortening of the lesser curvature (Fig. 3).

The pathological report was as follows: "The pyloric antrum shows an injected mucosa with thickening of its walls. The pylorus is highly stenosed by an annular fibrous mass. The lesser curvature is thickened and a round ulceration, 0.6 cm. in diameter, was noted therein proximal to the stenosis. Microscopic sections show erosion of the lining mucosa which is replaced by many thrombosed, thin-walled blood vessels. Beneath the submucosa and extending into the musculature there are areas of fibrosis and atrophic muscle fibers. There are also many areas of inflammation as manifested by plasma cells, lymphocytes, and monocytes.

Pathological diagnosis:—"Pyloric stenosis due to fibrosis, secondary to severe gastritis."

The patient made an uneventful recovery and has remained well since his discharge from the hospital.

Comment

Unlike stricture of the esophagus secondary to lye ingestion, pyloric stenosis due to fibrosis resulting from corrosive gastritis is not too well known. Strong alkalis, notably lye, produce coagulation of all tissues, but when swallowed chiefly affect the esophagus, invariably leading to subsequent fibrosis and stricture. In the stomach alkalis are quickly neutralized by the acid gastric contents, and therefore do not usually cause the extensive damage as do acid corrosives. Heindl[9], in a review of 160 cases of esophageal stricture due to lye, found pyloric stenosis present in 20 per cent of the cases. It is noteworthy that pyloric stenosis by lye occurs only in conjunction with involvement of the esophagus.

Acids, on the other hand, usually have only a superficial searing action on the esophageal mucosa. Associated esophageal stricture, however, has been reported in 20 per cent of the cases with predominantly gastric involvement[6].

In contrast to alkalis, acids produce a markedly corrosive effect on the delicate columnar epithelium of the stomach. Flowing down the lesser curvature and pooling in the antrum, aided by pylorospasm, the corrosive acid exerts its destructive effects almost exclusively in these areas. The damage is more extensive when the stomach is empty, due to the obvious lack of dilution and protection by food.

The most dangerous complication of swallowing corrosive acids is an acute destruction and perforation of the gastric wall with peritonitis. Another serious complication is massive gastric hemorrhage and shock, which usually occurs within a few days after the onset, as happened in the present case.

The late sequel of pyloric stenosis may begin from a few weeks to several months, usually 4 to 8 weeks, after the onset. It is due to the coagulation necrosis of the surface epithelium and submucosal tissue, with destruction of blood vessels, glands, and lymphatics, and finally fibrosis and scarring. There may result pyloric stenosis, tubular narrowing of the antrum, *linitis plastica*, or hour-glass constriction.

Although hydrochloric acid is the most frequent agent in the reported cases of pyloric stenosis, sulfuric acid is probably more commonly used, but few survive its initial insult. Besides hydrochloric acid, sulfuric acid and lye, other corrosives that have been implicated include nitric acid, phenol, trichloracetic acid, zinc chloride, copper sulfate, formaldehyde, and ferrous sulfate. Strange et al[10] reported a case in which the corrosive used was Clorox (a 5¼ per cent solution of sodium hypochlorite in water). In most of the reported cases the corrosive agent was taken with suicidal intent. In several instances, when it was taken accidentally, it was mistaken for whiskey, which probably happened in our case.

Management of the acute initial phase of corrosive gastritis, as outlined by Steigmann and Dolehide[8], consists of recognized supportive measures, including sedatives, antispasmodics, antibiotics, blood transfusions, fluids, electrolytes, and various demulcents, as egg-white, milk and olive oil. These authors warn of the obvious danger of using a large stomach tube. In selected cases they advise a specific antidote, such as a weak alkaline solution for acids, saline solution for silver nitrate and alcohol for phenol.

Those cases that survive the initial insult may enjoy good health for weeks or even months. Most of them, however, subsequently develop the characteristic vomiting, weight loss and electrolyte imbalance due to the development of pyloric obstruction secondary to fibrosis.

The diagnosis is readily made by the roentgen findings of a smoothly outlined stricture of the pyloric antrum, which, in the absence of the knowledge of a history of acid poisoning, might easily be misinterpreted as representing malignancy[7]. The gastric analysis usually shows absent or low free hydrochloric acid.

The treatment of the well established pyloric stenosis is obviously surgical. The type of operation depends on the extent of the pathology found, the physical condition of the patient, and the ability and judgment of the operating surgeon. Pyloroplasty, gastroenterostomy and subtotal gastrectomy have all yielded satisfactory results.

Conclusion

A case of corrosive gastritis in a 33-year old white male, with subsequent development of pyloric stenosis, has been presented. The corrosive agent was hydrochloric acid. Treatment was by subtotal gastrectomy with excellent results.

The literature of this condition has been reviewed.

The pathology and management of early and late phases have been discussed. Attention is called to the possibility of misdiagnosing the roentgen findings of pyloric stenosis as being due to carcinoma in the absence of a history of swallowing a corrosive agent, usually an acid.

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HYPERVITAMINOSIS A—TOXIC REACTION*

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Although the toxic effects of excess Vitamin A in children and in experimental animals has been increasingly studied and reported in the literature in the past decade, less attention and publicity have been given to such an entity in adults. Until the report of Elliott and Dryer in the *Journal of the American Medical Association* on 21 July 1956, only four cases of chronic hypervitaminosis A had been reported in adults[1,2,3,4]. The amount of Vitamin A necessary to produce toxic symptoms undoubtedly varies because of numerous factors that are subject to physiological variations in human beings, and to pathologic factors. We wish to report three such cases of chronic hypervitaminosis A, with clearing of symptoms when the excess vitamin intake had been discontinued.

Case 1:—A 16-year old white girl was first seen in August of 1953 because of acne vulgaris. In addition to dietary and local therapy, Vitamin A in the form of Aquasol A, 50,000 units, three times a day, was prescribed. She was next seen in October of 1953, at which time the acne was much improved, and she was instructed to take Vitamin A, 50,000 units, twice a day. On her own initiative, however, she continued to take 150,000 units of Vitamin A daily, although not under medical supervision until November of 1955. At this time it was noted by her family that the patient was losing her hair, and we were so notified. The Vitamin A intake was immediately discontinued. The patient was not seen in the office until December of 1955, when she stated that the loss of hair had slowed considerably. In January of 1956, she stated that the hair had stopped falling out. When last seen in March of 1956, however, she stated that she still had less than the normal amount of hair, and by communication in April of 1957 she informed us that the hair had never returned to its original amount. In addition to the hair loss, the patient stated that in August of 1954 the menstrual cycle changed and from that time until the Vitamin A was discontinued in November of 1955, her periods occurred only about every two months whereas previously they had been quite regular with the 28-day cycle. The flow had become much less and the periods lasted only about four days instead of the usual seven to eight days. She had also suffered from marked anorexia, and

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had lost considerable weight. Shortly after the disturbance in the menstrual cycle, she began to have epistaxis for no known reason. This persisted until the discontinuance of Vitamin A. No laboratory work was possible since this patient was not seen in the office until after the Vitamin A had been discontinued for over a month.

Case 2:—A 47-year old white man, who was first seen in December of 1946 for general examination, gave a history of albuminuria for the previous 15 or 16 years. Physical examination at that time was within normal limits, as were the usual laboratory studies except for 1 plus albumin in the urine. When next seen in December of 1951, he complained of generalized dry, eczematoid dermatitis, particularly of the legs. Again, except for the dermatitis, a lipoma on his back and moderate varicose veins of the left leg, his physical examination was normal. The lipoma was removed surgically, and saphenous ligation with stripping was performed on the left leg. His recovery was uneventful. At this time the patient was given Vitamin A, 200,000 units daily, in the form of Aquasol A. Because his skin was so much improved, he continued to take the Vitamin A in this dosage until 5 April 1954. On 30 March 1954 he noticed what appeared to be a bruised area on the left lower leg, and five or six days later, a similar bluish area on the flexor surface of the right arm. Because there was no history of injury to these areas, he came to the office to be examined, and on the day of admission another large ecchymotic area appeared above the knee on the inside of the left leg. The above described areas, on examination, appeared ecchymotic and there were petechial hemorrhages on the buccal lining of the mouth. There were also two poorly defined yellowish erythematous plaques on the left lower leg. Microscopic examination of tissue removed for biopsy of one such plaque showed findings compatible with a diagnosis of parapsoriasis.

The following laboratory tests were normal: complete blood count, prothrombin time, blood sedimentation rate, Coombs' test, VDRL, bone marrow studies, chest, gallbladder and gastrointestinal x-rays, and an electrocardiogram. The blood platelets were 100,000. The blood nonprotein nitrogen was 47 mg. per cent. The blood clotting time was three minutes, but the bleeding time showed continued bleeding after 30 minutes. A urinalysis showed a reaction of 6.5, specific gravity of 1.020, 4 plus albumin, an occasional white blood cell and 2 plus red cells, with an occasional hyaline cast. Clot retraction time showed only beginning retraction in two hours, with imperfect retraction at the end of 24 hours. The Vitamin A was discontinued and three weeks later the clotting time was six minutes and the bleeding time was one minute. The blood platelets at that time were 147,000. The blood nonprotein nitrogen was 37 mg. per cent. The clot retraction time was normal. The hemorrhagic spots had disappeared, including those on the mucous membranes of the mouth. Except for chronic albuminuria, the patient has remained well since that time, and has had no further hemorrhagic tendency.

Case 3:—A 67-year old white man, was seen because he had noticed a tendency to bleed easily for five or six years. On direct questioning, it was learned that he had been given a daily dosage of 100,000 units of Vitamin A by an ophthalmologist approximately six years previously and since he had found this to be helpful he decided to double the amount, and had been taking 200,000 units daily until three months prior to admission. He stated that he had bled intermittently from the gums for three or four years, and two years previously he had had profuse bleeding during dental extractions. He had again bled seriously five months previous to admission, with further extraction of teeth.

Physical examination revealed the skin to be flushed, dry and scaly. The right eye had been enucleated. The left eye was normal, except for minimal arteriosclerotic changes in the retinal vessels. He had mild emphysema with mild hypertension shown by the blood pressure of 166/88. The balance of the physical examination was not remarkable.

The following laboratory tests were normal: complete blood count, bleeding and clotting time, prothrombin time, clot retraction, cephalin flocculation, total protein and A/G ratio, blood calcium and urinalysis. The blood nonprotein nitrogen was 45 mg. per cent. There was 14 per cent retention of the bromsulfalein dye in 45 minutes.

The only other medication taken during this period by the patient was testosterone in the form of Oreton, 25 mg. intramuscularly, two or three times weekly. Four months after the discontinuance of the Vitamin A, the remaining teeth were extracted without unusual bleeding. He has had no further hemorrhagic tendencies and on a recent occasion he stated that he was asymptomatic.

Comment

Because Vitamin A in doses such as those cited here often may be used for short periods in the treatment of acne vulgaris and other lesions, the nature of which suggest a Vitamin A deficiency, we have felt it wise to suggest the possible toxic effects of overdosage. In the cases presented, such high dosage was maintained from two to six years. In one of the cases loss of hair was the chief manifestation, while in the other two cases bleeding or hemorrhagic tendencies were most prominent. Facilities for Vitamin A blood levels were not available on these patients, but the amelioration of symptoms with the cessation of Vitamin A intake was felt to be justification to call attention to these cases. The mechanisms by which such toxic manifestations occur are being more widely studied[5]. In the meantime, it is hoped that calling attention to these toxic manifestations may prevent further abuse of self treatment and by the many nonqualified proponents of large vitamin intake as a panacea.

SUMMARY

Three adult patients with toxic manifestation from prolonged and excessive ingestion of Vitamin A are presented. The positive physical findings were those of alopecia, anorexia, malaise, petechial and ecchymotic hemorrhages into the skin and mucous membranes. These toxic manifestations disappeared upon discontinuing the Vitamin A intake and have not recurred.

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SYMPTOMATIC RELIEF OF NAUSEA AND VOMITING WITH TRILAFON® (PERPHENAZINE): A PRELIMINARY REPORT

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Nausea and vomiting are among the most frequently encountered symptoms in gastroenterologic practice. The etiology may be emotional, a minor illness, or advanced malignancy; therefore, treatment of hyperemesis will be based on its cause. Symptomatic treatment, however, is indicated to relieve and, in some instances temporarily, to overcome or alleviate discomfort.

Many drugs have been used to control hyperemesis. Most recently, some derivatives of phenothiazine, best known for their tranquilizing effects, have been used also as antiemetics. Chlorpromazine was the first of these compounds to be synthetized and early results were extremely encouraging, however, this preparation occasionally may produce serious side-effects (hypotension, jaundice, and agranulocytosis).

Continued experimentation has produced newer analogues which offer equal if not greater effectiveness and few undesirable sequela.

Perphenazine (Trilafon), a new amino derivative of chlorphenothiazine, has shown encouraging results in laboratory[1-4] and early clinical[5-8] evaluation. These reports encouraged us to evaluate Trilafon among our patients.

Method

We administered Trilafon, orally and parenterally, to 110 patients with gastrointestinal diseases.* The drug was used for symptomatic relief of nausea, vomiting, and abdominal distress while we attempted to arrive at a definitive diagnosis of the underlying disorder. The usual dose was 4 or 8 mg. three times daily.

We also administered indistinguishable placebos alternately with Trilafon in some cases so that the effect of the drug could be evaluated objectively.

*J. Black, M.D., Division of Clinical Research, Schering Corporation, Bloomfield, New Jersey, provided the Trilafon and the placebos for this study.

Results

Most of our patients responded rapidly. Nausea and vomiting were usually relieved within 24 to 48 hours; in chronic conditions, improvement could usually be maintained on reduced doses. The placebos were ineffective. There were no side-effects except occasional drowsiness when 24 mg. or more of Trilafon was administered daily.

The following 11 case reports are representative of this series.

Case 1:—Female, 69 years, 208 pounds, blood pressure 170/90. An acute episode of nausea and vomiting occurred after a long bus trip. Trilafon, 12 mg. daily, was administered in 3 preprandial doses for 3 days. Relief occurred within 24 hours after therapy was begun.

Case 2:—Male, 26 years, 138½ pounds, blood pressure 122/80. The patient had had intermittent rectal bleeding for 10 years. An episode of rectal bleeding, nausea, and vomiting followed a severe emotional upset. After gastrointestinal x-ray examination a diagnosis of hypermotility, spasm and irritable colon was made. Symptoms disappeared after a week of therapy with Trilafon, 24 mg. daily in 3 divided doses.

Case 3:—Male, 67 years, 157½ pounds. This patient had a peptic ulcer and was being maintained on an antiulcer regimen. Trilafon, 4 or 8 mg. 3 times daily, was administered for an acute episode of nausea, vomiting, and abdominal cramps but no relief occurred.

Case 4:—Female, 42 years, 93½ pounds, blood pressure 148/82. This highly neurotic patient was hospitalized because of duodenal ulcer, heartburn, nausea, vomiting and dehydration. Parenteral administration of Trilafon did not control the hyperemesis, but 32 mg. Trilafon daily, orally in 4 divided doses, afforded some relief and the patient was able to retain nourishment. Improvement continued with Trilafon and antiulcer medication, and the patient was discharged. The weight had increased to 98 pounds. On an ambulatory antiulcer regimen further weight gain and improvement occurred.

Case 5:—Female, 30 years, 150 pounds, blood pressure 138/70. Several months previous, benign adenomas had been removed from the right lobe of the thyroid. When seen the patient was 5 months' pregnant and extremely nervous, she complained of nausea, vomiting, and palpitations. Trilafon, 12 mg. daily in 3 preprandial doses, was administered. Relief of tension, nausea, and emesis occurred within 24 hours. An uneventful pregnancy with normal delivery followed.

Case 6:—Female, 65 years, 137 pounds, blood pressure 128/82 to 140/82. This patient had a history of avitaminosis and weight loss, which responded to revision of the diet and administration of ascorbic acid. An episode of nausea was treated with Trilafon, 1 c.c. parenterally, which proved ineffective. The

patient was hospitalized because of continued gastrointestinal distress and after gastrointestinal and gallbladder series, a diagnosis was made of calculi in the gallbladder and common bile duct.

Case 7:–Male, 48 years, 133 pounds, blood pressure 130/70. Five years previously the patient had a subtotal gastrectomy for peptic ulcer, followed by the dumping syndrome, nausea, vomiting, weight loss, and dehydration. Trilafon, 24 mg. daily in 3 preprandial doses, was administered for 10 days; symptoms were relieved and general improvement occurred gradually. He was given placebos resembling the Trilafon tablets and told to take them while remaining free from symptoms; if symptoms recurred, he was to take the tablets which actually contained Trilafon. The patient made a satisfactory recovery and takes the tablets only occasionally. He is able to distinguish between the placebo and Trilafon and finds the former ineffective.

Case 8:–Female, 28 years, 121¼ pounds, blood pressure 120/70. This patient is emotionally upset because of the psychiatric illness of her child. She presented numerous complaints, including epigastric pain and nausea. Gastrointestinal examination revealed marked ptosis of the viscera but no other pathology. Placebos were given, with no effect. Spasm, nausea, and tension diminished when 12 mg. Trilafon daily was administered; when the placebos were substituted, symptoms recurred. The patient was then instructed to take 4 mg. Trilafon once or twice daily, as needed. Currently improvement is being maintained on 4 mg. Trilafon daily.

Case 9:–Male, 42 years, 133 pounds, blood pressure 140/80. This patient has been ill for 1 year, following an operation for a penetrating duodenal ulcer. There was a weight loss of 30 pounds accompanied by weakness, anorexia, dehydration, dumping syndrome, and pruritus ani. Trilafon, 20 mg. daily preprandially and before bedtime, effected a temporary improvement in the gastrointestinal symptomatology. Dosage was increased to 24 mg. daily, and the patient was instructed to alternate the 24 mg. schedule with a 12 mg. schedule. Improvement continues; the patient is less irritable and experiences the dumping syndrome only occasionally when subjected to emotional stress.

Case 10:–Female, 59 years, 174 pounds, blood pressure 132/80. This extremely apprehensive patient has multiple diverticula of the colon, cholecystitis, chronic duodenal ulcer, and a movable left kidney. She had an acute episode of severe abdominal distress which she attributed to eating fruit with seeds. Local treatment for the rectal distress and a bland diet were prescribed. She was given 8 mg. Trilafon and placebos and told to alternate the tablets daily. The placebos afforded no relief but Trilafon rapidly relieved the nervous tension, spasm, and pain.

Case 11:–Male, 51 years, 150 pounds, blood pressure 125/80. The patient has a 20-year history of abdominal distress. In 1955 a hemorrhoidectomy was

performed and the patient was advised to change his job, which he did after considerable emotional distress. Episodes of belching, vomiting, bloating, and bowel dysfunction occurred intermittently. A diagnosis of intrinsic gastric defect was made and extensive surgery was performed. During the protracted convalescence, cramps and abdominal distention persisted. Trilafon, 12 to 24 mg. daily, provided some relief but gas and diarrhea persist. He takes 4 or 8 mg. Trilafon occasionally as needed.

Summary

Trilafon, a phenothiazine derivative with marked antiemetic properties, was administered to 110 patients for symptomatic relief of nausea and vomiting. The usual dosage schedule was 12 to 24 mg. daily in 3 preprandial doses. Control studies were conducted in some patients by alternating Trilafon with indistinguishable placebos. Nausea and vomiting were relieved rapidly in most patients. There were no side-effects except occasional drowsiness among patients who received 24 mg. or more daily. Eleven cases are reported in detail.

Conclusion

Trilafon is a safe and effective agent for the control of nausea and vomiting in patients with gastrointestinal disease.

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EFFECTS OF A NEW SPASMOLYTIC-SEDATIVE IN THE TREATMENT OF 50 CONSECUTIVE HOSPITALIZED GASTROINTESTINAL CASES

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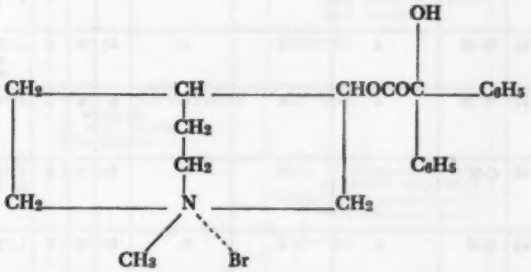
A new spasmolytic compound, clidinium bromide, (1-methyl-3-benziloyl-oxyquinuclidinium bromide), has been found to have methantheline-like activity. The structural formula is:



Laboratory studies have shown the spasmolytic effectiveness of the new compound (henceforth to be referred to as "Marplan" for brevity) to be equal to that of atropine and methantheline on the basis of tests for antiacetylcholine activity on isolated rabbit intestine. In normal unanesthetized dogs, with a balloon recording apparatus inserted through fistulas in the stomach and ileum, 1.0 mg./kg. i.v. of Marplan® produced the same degree of relaxation as 0.1 mg./kg. atropine, and the duration of activity was one-half as long. Also, in the rabbit, 0.5 mg./kg. i.v. of Marplan decreased the motility of the stomach and intestine 35 minutes. In still another experiment, using guinea pigs with a mecholyl-induced bronchospasm, atropine protected half the animals at a dose of 0.05 mg./kg., Marplan protected at 0.2 mg./kg., and methantheline protected at 0.3 mg./kig. Marplan in this particular test, therefore, is one-fourth as strong as atropine and equal to methantheline. The LD_{50} intravenously in the dog has been demonstrated to be 26 mg./kg.[1]

Since the first report in 1950, evaluating anticholinergic drugs for treating peptic ulcer, many quaternary ammonium compounds have been created and used[2,3,5,7,8]. The applicability of these compounds in gastrointestinal disorders, more especially as related to parasympathotonia and suppression of gastric se-

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TABLE

No.	Patient	Age	Color and sex	Dose No. tablets taken per 24 hours	Xerostomia	Cycloplegia	Bladder atony	Tachycardia	Stomatitis and constipation	Clinical Diagnosis
1	T.H.C.	32	W-M	4	0	0	0	0	0	1. Anxiety reaction without evidence of organic disease 2. Psychoneurosis
2	L.P.G.	25	W-M	4	0	0	0	0	0	1. Functional gastrointestinal disease (with nausea, pyrosis, mild epigastric pain)
3	C.L.H.	61	W-M	4	0	0	0	0	0	1. Chronic nonspecific gastritis
4	L.J.	48	C-M	4	0	0	0	0	0	1. Duodenal ulcer 2. Essential hypertension
5	J.M.L.	43	C-M	4	0	0	0	0	0	1. Duodenal ulcer, active
6	F.M.	37	C-M	4	0	0	0	0	0	1. Chronic duodenal ulcer with active bleeding 2. Pyloric inflammation
7	G.M.M.	25	W-M	4	0	0	0	0	0	1. Bleeding duodenal ulcer
8	R.P.V.	39	W-M	4	0	0	0	0	0	1. Prepyloric ulcer 2. Duodenal ulcer 3. Peripheral neuropathy, Multiple
9	A.L.W.	34	W-M	4	0	0	0	0	0	Functional gastrointestinal disease (with nausea and mild epigastric pain)
10	W.H.W.	30	W-M	4	0	0	0	0	0	Functional gastrointestinal disease (with nausea, vomiting, weight loss, nervousness)
11	G.K.W.		W-M	4	0	0	0	0	0	Functional gastrointestinal disease (with epigastric pains)
12	C.C.D.	41	W-M	8 originally 4 finally	3+ on "8" 0 on "4"	3+ on "8" 0 on "4"	0	0	0	1. Duodenal ulcer without x-ray evidence 2. Anxiety reaction
13	D.J.P.	36	W-M	8	0	0	0	0	0	Duodenal ulcer
14	W.O.A.	56	W-M	8	0	0	0	0	0	Esophageal hiatus hernia
15	W.B.B.	51	W-M	8	0	0	0	0	0	Gastric ulcer, benign

Pertinent x-ray findings	Pertinent laboratory findings	Results and Miscellaneous comments	Inclusive hospitalization dates (for therapy)
Coarsening of rugal folds of stomach and duodenal bulb	Normal (including liver function studies)	No benefit from therapy Patient later received insulin shock treatment with benefit	7/ 2 /56— 7/15/56
Normal (incl. gastrointestinal series)	Normal	Improved	10/ 8 /56—10/19/56
Normal (incl. gastrointestinal series)	No free HCl on gastric analysis 28 total acidity Rest normal	Improved	10/ 1 /56—10/30/56
Gastric diverticulum lesser curvature stomach at cardia Active duodenal ulcer	Normal	Pain in epigastrium not controlled with M-N (Changed to methantheline with control of pain)	10/10/56—10/26/56
Prolapsed gastric mucosa into base duodenal bulb Active duodenal ulcer	Normal	Improved	9/26/56—10/15/56
Active duodenal ulcer	Normal	Unimproved on medical regimen including antacids Cured with surgery	7/ 7 /56— 8/ 1 /56
Tender over epigastrium but no niche seen on upper gastrointestinal x-rays Normal gastroscopy	Normal (incl. G. T. T. and gastric analysis)	Unimproved (pain controlled with methantheline)	10/ 2 /56—10/26/56
Prepyloric and duodenal ulcers	1. No free HCl on gastric analysis 2. Blood-loss type anemia 3. Normal CSF on L.P. 4. Normal bone and muscle biopsies 5. 15% BSP retention initially but this dropped to normal later during hosp.	Improved	7/ 5 /56—11/21/56
Scarring lesser curvature duodenal bulb (Had perforated peptic ulcer with surgical repair—1946)	Normal	Improved	9/ 4 /56— 9/13/56
Normal (incl. gastrointestinal series)	Normal	Improved	10/ 2 /56—10/13/56
Normal (incl. gastrointestinal series)	Normal	Improved (phenobarbital added due to nervousness)	10/ 3 /56—10/16/56
Normal (incl. gastrointestinal series)	Normal	Improved	2/ 5 /57— 2/18/57
Deformed duodenum with pseudo-diverticulum Greater curvature without niche	Normal	Improved	1/15/57— 2/ 5 /57
Esophageal hiatus hernia	Normal	Improved	1/30/57— 2/21/57
Gastrointestinal x-rays normal x 2 Lesion identified and followed gastroscopically	"0" Free HCl—Rest normal	Improved	12/31/56— 2/ 6 /57

TABLE I

No.	Patient	Age	Color and sex	Dose No. tablets taken per 24 hours	Xerostomia	Cycloplegia	Bladder atony	Tachycardia	Stomatitis and constipation	Clinical Diagnosis
16	J.E.C.	22	C-M	8 initially 4 finally	0	0	0	0	0	Functional gastrointestinal disease
17	R.J.D.	39	C-M	4	0	0	0	0	0	Duodenal ulcer with pyloric obstruction
18	J.B.H.	33	W-M	4	0	0	0	0	0	Observation for gastrointestinal disease—None found
19	I.C.J.	39	W-M	4	0	0	0	0	0	Epigastric pain—Functional (Old subtotal gastrectomy for duodenal ulcer)
20	C.L.N.	31	W-M	8 initially 4 finally	4+ 0	0 0	3+ 0	0 0	0 0	Functional gastrointestinal disease Bronchial asthma
21	D.E.G.	25	W-M	4	0	0	0	0	0	Probable duodenal ulcer Pylorospasm Upper gastrointestinal bleeding
22	D.G.	40	C-M	4	0	0	0	0	0	Duodenal ulcer
23	C.A.L.	32	W-M	4	0	0	0	0	0	Functional upper gastrointestinal complaints
24	G.W.H.	61	W-M	4	0	0	0	0	0	1. Duodenal ulcer 2. Parkinsonism 3. A.-S., generalized
25	V.M.W.	31	C-M	4	0	0	0	0	0	Duodenal ulcer
26	L.F.W.	46	W-M	4	0	0	0	0	0	Diverticulosis of sigmoid colon
27	J.G.B.	33	W-M	8	0	0	0	0	0	Esophageal hiatus hernia
28	E.D.D.	38	W-M	4	0	0	0	0	0	Duodenal ulcer
29	M.L.S.	32	W-M	4	0	0	0	0	0	Duodenal ulcer
30	N.D.T.	34	W-M	4	0	0	0	0	0	Duodenal ulcer with possible posterior penetration
31	A.G.W.	56	W-M	4	0	0	0	0	0	Duodenal ulcer, causing obstruction Operated (Posterior gastrojejunostomy)
32	N.J.W.	30	W-M	4	0	0	0	0	0	1. Duodenal ulcer 2. Undiagnosed disease characterized by migratory joint pains
33	C.V.B.	37	W-M	4	0	0	0	0	0	1. Duodenal ulcer 2. Physiologic gastrointestinal reaction manifested by vomiting
34	L.E.T.	35	W-M	4	0	0	0	0	0	Duodenal ulcer
35	H.S.B.	29	W-M	4	0	0	0	0	0	1. Duodenal ulcer 2. Anxiety reaction

(continued)

Pertinent x-ray findings	Pertinent laboratory findings	Results and Miscellaneous comments	Inclusive hospitalization dates (for therapy)
Normal (incl. gastrointestinal series)	Normal	Improved	2/11/57— 2/26/57
Same as clinical diagnosis	Normal	Subtotal gastrectomy (Hofmeister retrocolic antiperistaltic)	12/10/56— 1/11/57
Normal (incl. gastrointestinal series)	Normal	Improved	2/ 5 /57— 2/15/57
Normally functioning postoperative stomach Normal gastroscopy	Normal ("0" free HCl postoperatively)	Unchanged	10/ 4 /56— 1/29/57
Normal B. E. and chest films No upper gastrointestinal series done	Normal	Improved	2/12/57— 3/ 1 /57
Pylorospasm, diverticulum second portion duodenum	Normal	Improved	10/18/56—10/30/56
Ulcer crater lesser curvature duodenum	Normal	Unchanged (pain controlled with Tridihexethyl iodide)	10/23/56—11/15/56
Normal (incl. 2 upper gastrointestinal series)	Normal	Improved	11/19/56—12/ 7 /56
Spasticity and irregularity of duodenal bulb without niche	Normal	Improved	12/ 4 /56—12/21/56
Normal (incl. gastrointestinal series)	Normal	Improved	10/ 8 /56—10/19/56
Normal upper gastrointestinal series Diverticulitis of sigmoid and lower colon	Normal	Gradually improved	10/17/56—11/ 2 /56
Same as clinical diagnosis	Normal	Improved	12/ 7 /56—
Duodenal irregularity without definite niche	Normal	Improved	10/19/56—11/16/56
Pylorospasm, spastic cecum on upper gastrointestinal series Normal cholecystogram	3+ ceph. floc. 11,800 WBC Rest normal	Improved	11/ 5 /56—12/ 1 /56
Irregular duodenum with pseudodiverticulum greater curvature side near base with ulcer niche in center of bulb	14,800 WBC Rest normal	Improved (pain controlled better with Methantheline)	7/ 3 /56— 7/31/56
Scarred duodenal bulb, with adhesions	Normal	Improved (pain controlled better with Methantheline) No definite ulcer detected at surgery	7/ 2 /56— 8/10/56
Deformed duodenal bulb	Normal (incl. G. T. T.)	Improved	10/24/56—12/12/56
Pylorospasm with spastic duodenal bulb No definite ulcer niche	Normal	Improved	7/ 9 /56— 7/20/56
"Clover-leaf" deformity of duodenum with ulcer niche in posterior bulb	Normal	Improved	7/ 4 /56— 7/24/56
Deformed duodenal bulb consistent with diagnosis of duodenal ulcer	Normal—except positive S. T. S.	Improved	7/13/56— 7/27/56

TABLE

No.	Patient	Age	Color and sex	Dose No. tablets taken per 24 hours	Xerostomia	Cycloplegia	Bladder atony	Tachycardia	Stomatitis and constipation	Clinical Diagnosis
36	N.D.T.	34	W-M	4	0	0	0	0	0	Duodenal ulcer with mild hemorrha and probable posterior penetrati
37	J.A.M.	35	C-M	4	0	0	0	0	0	Duodenal ulcer with hemorrhage
38	C.L.J.	40	C-M	4	0	0	0	0	0	Psychophysiologic gastrointestinal reaction, with belching, p.c. fullness, fatty food intol. and "lump" in epigastrium
39	C.M.E.	24	W-M	4	0	0	0	0	0	Duodenal ulcer with hemorrhage
40	J.H.C.	30	W-M	4	0	0	0	0	0	Duodenal ulcer
41	E.B.W.	59	W-M	4	0	0	0	0	0	1. Psychophysiologic gastrointestin reaction with nervousness, exce sive gaseousness, and flatus 2. A.S.H.D. with old anterior m cotic infarction, healed
42	R.L.P.	34	W-M	4	0	0	0	0	0	Duodenal ulcer
43	E.T.L.	60	W-M	4	0	0	0	0	0	1. Gastrointestinal hemorrhage, mil probably due to bleeding margin ulcer 2. Aortic stenosis 3. Inguinal hernia, right, indirect 4. B.P.H.
44	C.C.C.	47	W-M	4	0	0	0	0	0	Duodenal ulcer
45	J.H.D.	44	W-M	4	0	0	0	0	0	Pancreatitis, chronic, relapsing
46	W.E.H.	57	W-M	4	0	0	0	0	0	Anxiety reaction with somatic com plaints, tremor, inability to wo Duodenal ulcer, inactive, with scarring Pylorospasm
47	W.L.S.		W-M	4	0	0	0	0	0	Duodenal ulcer, chronic, active
48	O.P.R.	33	W-M	4	0	0	0	0	0	1. Psychophysiologic gastrointestin reaction (vague abdominal pain, gas, nausea, slight constipation 2. Exog. obesity 3. Right testicular atrophy (old mumps?)
49	A.O.H.	61	C-M	4	0	0	0	0	0	1. Gastric ulcer, benign 2. Emphysema, chronic
50	C.V.B.	36	W-M	4	0	0	0	0	0	1. Duodenal ulcer

ontinued)

Pertinent x-ray findings	Pertinent laboratory findings	Results and Miscellaneous comments	Inclusive hospitalization dates (for therapy)
iche in bulb with pseudodiverticulum on greater curvature side duodenum	Normal	Improved	7/ 8 /56— 7/31/56
regular duodenal bulb consistent with duodenal ulcer	Normal	Improved (500 c.c. blood needed to normalize hematocrit)	7/ 5 /56— 7/19/56
ormal (incl. upper gastrointestinal series)	Normal—except positive S. T. S.	Improved	7/ 9 /56— 7/26/56
arrowing duodenal bulb at apex ylorospasm	Normal	Improved	7/ 9 /56— 7/27/56
ıcer crater on anterior wall near base pasticity	Normal	Improved	7/13/56— 7/21/56
ormal cholecystogram and barium meal	Normal	Improved	7/11/56— 7/18/56
regular large rugal folds with rapid emptying o definite ulcer seen	Normal	Improved	7/ 4 /56— 7/18/56
ormal partial gastrectomy astroscopy negative	Normal	Improved	7/ 5 /56— 7/20/56
uodenal irregularity in outline, never filling well	Normal	Improved	7/10/56— 8/ 7 /56
ormal abdominal scout films and barium meal	Normal	Improved	7/ 9 /56— 7/24/56
d scarred duodenal bulb with clover-leaf formation and pseudodiverticulitis on greater curvature	Normal	Improved	5/21/56— 6/14/56
arrowing in distal portion duodenal bulb, with irregularity along lesser and greater curvature aspects o niche seen	Normal	Improved	8/14/56— 8/25/56
ormal (incl. chest, B. E. and upper gastrointestinal series)	Normal	Improved	6/26/56— 7/ 3 /56
astric ulcer lesser curvature at angularis (also seen on gastroscopy) epeat x-rays showed final disappearance of the lesion He had wedge resection for gastric ulcer 1955—hence this considered recurrence)	Normal	Improved	7/ 9 /56— 8/24/56
arsened duodenal bulb with spasticity of bulb, but no definite niche seen	Normal	Improved	7/ 9 /56— 7/20/56

cretion, have been reported many times. Ideally, there should be a selective block of acid secretion and peptic gastric activity and reduction of smooth muscle irritability, with the ultimate goal, of course, of relief from pain and satisfactory healing of the ulcer, if present.

Marplan was considered to represent a significant departure from the previously reported spasmolytic compounds and suggested interesting possibilities to us. A clinical study evaluating its effectiveness in consecutive unselected hospitalized patients with varied gastrointestinal complaints, therefore, seemed indicated. For this purpose Marplan was used in combination form with methyprylon (3,3-diethyl-5-methyl-2,4-piperidinedione), a mild sedative-hypnotic (henceforth referred to as "Noludar"). Each tablet used contained 50 mg. of Noludar® plus 5 mg. of Marplan.

Object of Study

The primary objective was to determine the clinical effectiveness of Marplan-Noludar in the treatment of peptic ulcer. Patients with functional disturbances of the gastrointestinal tract, however, were also included in the series.

Method of Study

Patients assigned to the Gastrointestinal Section of the McGuire Veterans Administration Hospital, Richmond, Va., were accepted for study in the order of admittance to the ward, with no prior selection. All subjects had been examined by the Admitting Physician on duty and considered eligible for hospital treatment on the Fifth (Gastrointestinal) Ward. White and colored patients of a wide age variation, but mostly in their early thirties, were included. No patients were followed in this series longer than termination of their hospitalization. No female patients were examined, inasmuch as none was accepted for hospitalization during this study. The over all duration of the project was made to include the so-called "good" and "bad" ulcer months, in an attempt to see if any variation in amount of medication or ultimate effectiveness might be detected. Dietary regimen, alkalis, and supportive therapy along standard ulcer therapy lines were given, where indicated, in conjunction with the Marplan-Noludar. No attempt was made at radical departure from accepted methods of treatment. If for some reason the Marplan-Noludar proved unsatisfactory, another drug was substituted, as is indicated in Table I. Laboratory work-up included the standard tests usually performed on a gastrointestinal ward.

Forty patients were white males, and 10 were colored males. The age range was from 22 years to 61 years, with most in their thirties. The diagnostic categories represented are as shown in Table II below. The number of tablets taken amounted to 4 per 24 hours (one a.c. t.i.d. and h-s.), except in four instances where the dosage was 8 per 24 hours (two a.c. t.i.d. and h-s.). It is interesting to note that three of these cases developed side reactions of a severity necessi-

tating reduction in dosage to half this amount. One patient tolerated the 8 tablets per 24 hours without any known side reactions. Side reactions included xerostomia, cycloplegia, and bladder atony. Tachycardia, stomatitis, and constipation were not detected in any of these 50 patients.

TABLE II

DIAGNOSIS IN 50 PATIENTS

Duodenal ulcer or probable duodenal ulcer	28
Functional gastrointestinal tract disease	14
Chronic nonspecific gastritis	1
Esophageal hiatus hernia	2
Gastric ulcer, benign	2
Diverticulosis of sigmoid colon	1
Pancreatitis, chronic, relapsing	1
Marginal ulcer, probable	1
	50

TABLE III

RESULTS

1. Unqualified improvement in 39 cases
2. Substitution of other similar-acting drugs needed in 4 cases (with satisfactory results being obtained)
3. Gastric surgery required in 2 cases
4. Insulin shock therapy given to a severe psychoneurotic case refractory to Marplan-Noludar and other similar-acting preparations
5. Unimproved in 4

From these findings it would appear that this preparation is well tolerated. Side-effects and undesirable reactions were absent in the majority, and mild in those few patients in which they did appear. These untoward effects were limited to those subjects receiving above-average doses and were readily controlled by dropping to the lesser but still effective dosage range. There would not appear to be too wide a dosage range, as optimum therapeutic results were achieved on the dosage of one tablet q.i.d. and most patients do not tolerate more than this.

Rather prompt and early relief from pain and distress of peptic ulcer was noted and similar results occurred in other organic gastrointestinal disorders associated with hyperacidity and hypermotility as well as functional or psychophysiologic gastrointestinal conditions. The specificity exhibited for its inhibitory effect on intestinal motility was considered especially satisfactory.

Although previous studies have shown Marplan to exhibit less local mydriatic activity than atropine, the presence of glaucoma should be considered a contraindication or a signal for caution[9]. Also, as with other drugs of this category, despite negligible or absent side reactions in our study, the drug should be used with caution in the presence of serious cardiac disease or prostatic hypertrophy.

Summary and Conclusions

1. A clinical evaluation of a new spasmolytic-sedative (Marplan-Noludar) has been made in 50 consecutive unselected hospitalized gastrointestinal cases.

2. Organic gastrointestinal disease as well as functional or psychophysiological gastrointestinal reactions were included in this study.

3. One tablet q.i.d. (containing 5 mg. Marplan and 50 mg. Noludar) was found to give optimum therapeutic effectiveness and to be relatively free of untoward side reactions. No serious toxic effects or side reactions were observed at this dosage level.

4. Marplan gives satisfactory results for disorders of the gastrointestinal tract associated with spasticity and increased motility, improvement having occurred in 39 of the 50 patients treated.

5. The dosage range is not as flexible as with certain other similar-acting preparations but this is not considered a serious drawback.

6. Glaucoma, prostatic hypertrophy, and serious cardiac disease should be considered contraindications or at least dictate the need for extreme caution.

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SERPASIL IN THE TREATMENT OF PEPTIC ULCER DISEASE WITH PSYCHOGENIC ETIOLOGY

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In a practice consisting largely of patients with digestive diseases, it is found that most were suffering from peptic ulcer, gastritis, or pyloroduodenal syndrome. During the period from November 1953 to June 1955, in approximately 60 per cent of these patients, at least one of the precipitating causes was believed to be a psychogenic factor in the patient's environment which produced or aggravated the gastrointestinal distress.

When these patients were first seen, organic damage usually had not progressed to the stage where surgery is necessary. Most cases were amenable to medical management, but must be regarded as having long-term recurring diseases[1,2], as well as acute conditions.

A review of the literature from the first description of peptic ulcer disease by Cruveilhier down through modern times, as well as actual experience over a period of time in treating these cases, teaches one of the existence of two basic premises: First, that peptic ulcers develop and recur on the basis of the quantity and strength of acid present. Secondly, in those patients who develop ulcers, a careful review of the precipitating factors reveals four major groups of causes which affect the lining of the digestive tract, either mechanically, through a hormonal mechanism, or through a central nervous system stimulation. These same factors can also cause recurrences, once the disease tendency is established.

1. *Improper eating habits:*—a. Mechanical factors, such as food that is improperly chewed, or too rough and scraping in its physical characteristics. b. Foods which are either irritating or cause hypersecretion, i.e., highly seasoned, fried foods, caffeine-containing beverages, or alcohol. c. By improper spacing of meals containing normal protein groups, which are capable of neutralizing gastric juice, so that the juice which accumulates with hunger may either erode the lining of the digestive tract, expanding minor abrasions and breaks in the mucosa, or constantly dissolve the surface of an ulcer which would otherwise heal.

2. *Infectious processes:*—Infectious processes, particularly upper respiratory infections in which there is a constant swallowing of pus, tend to precipitate ulcers and cause recurrences where the tendency to the disease is already present.

3. *Drugs:*—There are medications, such as the steroid hormones of the cortisone or ACTH group which delay healing or drugs such as aminopyrine,

salicylates, sulfonamides, and antibotics of the mycin groups, which cause recurrences by their working effect on gastric mucosa.

4. Psychogenic factors:—It is commonly accepted that, in addition to those psychic stimulations pertaining to food (thinking about it, smelling it, seeing it, or tasting it), other factors such as insecurity, hostilty, tension, aggravation and resentment can cause a stimulation of the parasympathetic system by way of the vagus nerve. This results in increased motility and spasm of the gastrointestinal tract and increased secretion of acid, thereby inducing or aggravating the peptic ulcer group of diseases.

In most cases of peptic ulcer in which it is possible to analyze the precipitating factors, it is found that there has been more than one possible cause. Of the four precipitating factors listed above, three are rather easily controlled: 1. The elimination of certain foods; proper spacing of meals. 2. Eradication of infection. 3. Elimination of certain drugs by the oral route, or markedly reducing the dosage.

A much more difficult factor to control is the constant interplay of stresses and tensions in the patient's environment. Simple anxieties may be allayed with reassurance, but deep-seated problems often must be tolerated for considerable periods of time. Any means by which the effect of the environment can be ameliorated will materially increase the number of active ulcers which may be healed by medical management and will decrease the rate of recurrences.

There are two general types of drugs which may be used to block the effect of emotional factors over the vagus pathways of innervation. The first is composed of those drugs which simply block the parasympathetic nervous pathways peripheral to the nervous system, such as Antrenyl, Banthine, Pro-Banthine, Monodral, Prantal, Atropine and the entire belladonna group of derivatives. The second group consists of drugs which act to reduce emotional tension and thus tend to decrease the activty of the autonomic nervous system. In this category are the barbiturates, chlorpromazine, and the various rauwolfia preparations, such as Serpasil.

The antiparasympathetic, or as they are generally termed anticholinergic, drugs have been widely used and are effective in promoting healing and preventing recurrences, but they have the disadvantage of neither preventing the anxiety reactions nor tranquilizing the patient.

An analysis of the characteristics of the second group of drugs suggests the following considerations:

Barbiturates:—The disadvantage of the barbiturates exists primarily in their habituating qualities when used for prolonged periods of time, and the difficulties encountered in withdrawing them. They also reduce the level of the patient's mental activity and efficiency so that his productive capacity is materially les-

sened. Their major action is to depress the patient mentally to a point where he can tolerate his anxieties and discomforts.

Chlorpromazine:—This is an effective drug when the psychogenic process is of true psychic proportions, such as acute alcoholism, obsessive psychoses, a major depressive reaction, or schizophrenia. It is also useful in cases of persistent nausea and vomiting, through the central blocking of these impulses. It has, however, three distinct disadvantages: It is the most expensive for the patient of the three groups of drugs on a maintenance level; second, it is comparable to the barbiturates in its general cerebral depressant effect, interfering with productive mental activity, and third, it may cause serious toxic effects such as jaundice and agranulocytosis.

Serpasil:—The rauwolfia group, and especially the single alkaloid reserpine (Serpasil), has several distinct advantages. Serpasil is intermediate in price (between the barbiturates and chlorpromazine), especially after a maintenance dose has been established. Its major advantage lies in its ability to tranquilize the patient so that he is aware of the surrounding aggravating factors, reacts normally to them, but is not upset and distracted by them. There is a distinct difference in action between reserpine and the barbiturates or the standard hypnotics used in the past to effect sedation. Reserpine is not a cerebral depressant[3,4]. The patient taking Serpasil is better able to concentrate and his productive work output is often increased rather than decreased, due to relief from distressing thought[5,6].

A major question arising in the use of Serpasil in patients with peptic ulcer disease appeared to be that of gastric secretion. Barrett et al, in studying the effect of reserpine on gastric secretion in the dog, concluded that reserpine evokes gastric secretion by stimulating the parasympathetic ganglia[7]. Clinical studies, particularly after parenteral reserpine, have also shown an increase in motility and the volume of gastric juice[8,9]. Theoretically, this would appear to be detrimental in the management of ulcer cases.

In the ulcer patient, however, if the degree of psychomotor activity were greatly reduced, less gastric secretion from psychogenic causes might more than offset any drug-induced secretion; and it would therefore be beneficial. Furthermore, if the diet is suitably adjusted to neutralize free acids in the stomach, it was felt that the drug might be effective. Lastly, if Serpasil were used in combination with other drugs known to reduce secretion, so that there would be no demonstrable increase in secretion, it was reasoned that its use in combination with proper diet and antiparasympathetic medication could materially augment the healing of active peptic ulcers stemming from psychogenic causes, and further, reduce the tendency to recurrences.

Approximately 60 per cent of the patients seen during this period were felt to have sufficient psychogenic factors in their environments to justify the

use of Serpasil. An attempt was made to analyze these factors and to group the patients according to the principal source of aggravation in each case. They were placed in seven major categories:

1. Occupational.
2. Economic insecurity.
3. Domestic and in-law.
4. Worry over illness of relatives.
5. Worry over continuous or itermittent pain (usually rheumatic or orthopedic).
6. Worry over the presence, or suspected presence of other serious illness.
7. Major psychoneuroses, psychoneurotic characteristics, or maladjustments.

No case was so classified unless the type and degree of tension was judged to be of significant proportion, either immediately, or over a period of time.

Under "Occupational" tensions were grouped those who worked long hours with over-responsibility, especially without commensurate authority; multiple aggravations, for example, salespeople who had to tolerate the idiosyncrasies of customers, shutting their resentment to them inside.

In the second category it seemed impossible to separate economic stress, such as the effect of long-term indebtedness or poor budgeting, from insecurity as a result of sudden retirement without previously accumulated funds, or without ways of augmenting an inadequate income, to which the patient had not become adjusted.

Under "Domestic and in-law" tensions were included incompatibilities between husbands and wives, parents and children, impending divorces, major differences in religion, drinking, sexual infidelities, or the necessity of tolerating unwelcome or meddlesome in-laws in the same household; also instances in which in-laws were attempting from outside the household to influence the patient or mate in their attitude towards each other.

In "Worry over illness of relatives", such factors as serious illness in near relatives often causes not only an increased mental burden, but the physical strain of actually caring for that relative.

In the fifth category, it has been found that prolonged pain, either of the primary ulcer disease if it has resisted diagnosis or treatment, or the pain of a secondary chronic disease which cannot be allayed immediately (orthopedic or rheumatic), creates a multiplicity of anxieties, phobias and fears, not only of the pain itself, but of future crippling. These patients often imagine nonexistent diseases and this can be a significant aggravating factor in causing recurrences or continuations of ulcer symptoms.

In the sixth group were those patients considered to have major worries due to serious parallel organic disease, such as gallstones requiring surgery, coronary attacks, malignancies, syphilis or diabetes, which was a source of constant worry over the present and future security of the patient.

In the last group were patients whose primary problem was one of psychoneurotic maladjustment. This included all those who were constitutionally inadequate to cope with their environment, or had major psychoneuroses not attributable to immediate temporary situations and which would be likely to be translated into all situations. Three patients in this category were of actual psychotic background of sufficient severity to have required shock treatment while under the care of a psychiatrist.

In studying the 99 patients in these groupings, it became apparent that anywhere from 2 to 4 of the 7 factors often paralleled each other. In analyzing the frequency of the individual psychosomatic factors, occupational tensions were a major factor in 38 of the 99 cases; economic insecurity in 54; domestic situations and in-law trouble in 30; ill relatives in 18; the existence of other serious disease in 23; problems of major psychoneurotic proportions in 29; and 3 had previously been diagnosed as psychotics. A summation of these figures totals more than 99, due to the multiplicity of factors in many of the patients. For example, one patient was known to have a marked aggravation from a nagging, overbearing wife who had a painful crippling arthritis. The wife's medical care required the expenditure of a considerable portion of the patient's salary and caused his indebtedness. At the same time, he was worried about his diabetic mother who had had a coronary infarction. At this time, he was suddenly promoted to a job as a section chief, which entailed pressure from his superiors and inferiors, with constant deadlines to be met. It was felt, in this case, that the aggravating factors must be equally divided between occupational, economic, domestic, and ill relatives.

Eighty-two patients with active gastric or duodenal ulcers were treated with an initial dose of 0.25 or 0.125 mg. Serpasil three times daily and an antiparasympathetic such as Antrenyl, Banthine, Centrine or Prantal. All patients were started on a liquid diet limted to 3 oz. of milk at half-hour intervals and as symptoms subsided the diet became more liberal being increased at two-week intervals through 4 successive stages until the fourth level or maintenance diet had been reached[10].

Within 30 hours, all except 6 of the 82 patients studied became completely free of pain. The regular dietary progress was maintained in these patients and there was no recurrence of symptoms. Patients have continued to remain asymptomatic and radiographic examinations have confirmed that all of the 76 patients have reached a state of clinical healing. None of the patients felt that there was a reduction in his mental ability or in his efficiency to perform normal work. In fact, in the cases of patients who were business executives whose occupations

involved considerable responsibility with multiple distractions, as a result of the lack of distraction and minor aggravations, their mental efficiency seemed to be increased.

Even though many of the original tension factors have continued to operate in these 76 patients and some additional factors, such as business reversals, impending divorces, or a death in the family have been added in some cases, there have been no recurrence of symptoms attributable to the gastrointestinal tract.

Of the 6 patients in whom results were judged to be unsatisfactory, the poor results in two were attributed to the patient's refusal to follow the diet or take medication and/or the intractability of the disease. These patients were eventually dropped from observation. In two others, there was no improvement in ulcer symptoms. Hence, in all fairness, it should be stated that these patients were victims of overbearing outside sources of tension and, in spite of diet and medication, there were intermittent recurrences of ulcer symptoms. Medication, however, was continued at the request of the patients since they felt that the severity and frequency of their stomach discomfort as well as their psychogenic tension was somewhat diminished.

In the other two cases, with poor results, there were prolonged periods of complete relief followed by intermittent periods of discomfort and ulcer activity. These patients revealed that they had omitted their medication from time to time and exceeded diet instruction when under stress. On resumption of proper diet and medication they experienced a relief of symptoms.

Conclusions

1. Anxiety, tension, insecurity, hostility and resentment, present in many patients with peptic ulcer disease, are factors stimulating gastric motility and secretion.

2. Although Serpasil (reserpine) alone has been found to increase gastric secretion in peptic ulcer patients, its tranquilizing effect particularly when it is given along with dietary and antacid therapy, has been found to be of considerable benefit.

3. All patients in this regimen were free of pain in 36 hours.

4. The recurrence rate in patients with healed ulcer is reduced when Serpasil is added to maintenance medication and diet.

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SPECIALISM IN THE DAYS AHEAD*

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On 6 June 1822, the Army Surgeon at the post of Mackinaw received an emergency call to the huddled waterfront at the foot of the hill. In the American Fur Company store a gun had been discharged accidentally and duckshot had entered the body of an 18-year old French-Canadian lad, causing a frightful wound—"a wound that never healed". The surgeon was William Beaumont and the lad was Alexis St. Martin.

Dr. Beaumont was called the "backwoods physiologist"[1] but he was a careful observer and a scientist whose thinking and reasoning established him as a first rate clinical investigator. His experiments formed a point of departure for modern research in gastroenterology; in fact, his curiosity and eagerness to learn about the various functions of the stomach, the gastric juice and the physiology of digestion led Beaumont to perform 238 experiments on Alexis and they were described in detail.

If anyone deserves to be nominated as a pioneer specialist in gastroenterology, Dr. William Beaumont would head the list. But, in any such discussion, one must not overlook St. Martin, who likewise contributed to science by permitting the experiments—experiments which caused him some discomfort and mental anguish. That these experiments were not harmful is attested by the fact that St. Martin lived to be 76 years of age. He married and reared a family and was a strong, healthy man. When he returned to Quebec from Mackinaw for the second time in 1831, he made the trip in an open canoe via the Mississippi and Ohio Rivers, Lake Erie, Lake Ontario and the St. Lawrence River. The family arrived in Montreal in June, having traveled more than 2,000 miles. Moreover, Alexis outlived Beaumont by 15 years.

In commenting upon his own work, Beaumont had this to say: "Truth, like beauty, when unadorned is adorned the most and in prosecuting experiments and inquiries, I believe I have been guided by its light."

The story of Beaumont and St. Martin has been told many times but it bears repeating because it illustrates what can be done when the spirit of inquiry is combined with the spirit of intellectual adventure in medicine.

One of the physicians who had a great interest in Beaumont and his experiments was Sir William Osler. Dr. Osler was a physician who was designated as a specialist or consultant in internal medicine, although he insisted that internal medicine was not a specialty but rather a vocation[2]. Let him tell

*Presented before the Annual Convocation of the American College of Gastroenterology, Boston, Mass., 20 October 1957.

you that internal medicine is "not itself a specialty (though it embraces at least a half a dozen), its cultivators cannot be called specialists, but bear without reproach the good old name physician, in contradistinction to general practitioners, surgeons, obstetricians, and gynecologists".

There are some who claim Dr. Osler as a gastroenterologist and the evidence for his special interest in this important system of the human body has been compiled and presented in an attractive and charming manner by Felix Cunha[3] in his essay entitled "Osler as a Gastroenterologist".

Specialization in medicine began to develop with the dawn of medical science and the scientific method. In the United States it began to emerge first in a primitive way about the middle of the last century. Shyrock[4] in his book "The Development of Modern Medicine" tells the story very well indeed.

After the war between the states, the enormous advances in medicine and the practical application of the ancillary sciences resulted in a legitimate growth and development of specialism. This had been foreshadowed earlier by the establishment in some of the Old World cities of hospitals for special diseases, such as the Royal Ophthalmic Hospital and the Royal Ear Hospital in London. Like every change in a profession, the leaders opposed specialism for a long time and Weir Mitchell once said that he could remember the day when to specialize was to embrace quackery and face ostracism. Until the beginning of this century, the special departments in our great hospitals were in charge of general physicians or surgeons on the staff of the hospital, the need for a specialty being thus admitted but with a compromise to prevent the creation of full time specialists. In this country, Dr. Halsted was the first surgeon or at least among the first to create the full time specialists in surgery although there were women's surgeons and men's surgeons prior to that time. The case for specialism is now universally recognized and, as a result of the intensive study thus made possible, and as a result of the upgrading of education, the standard of technical skill and medical practice has greatly improved, because as medical education goes, so goes medical practice. When one is improved and related to research and new knowledge, and viewed in biological perspective, then the quality of medical care is improved.

The rise of specialism and the improvement of medical care which followed has led to decentralization and the cleavage of medicine into separate compartments, frequently called divisions, departments or sections. This has led to a system of teamwork and organization within groups which has long been an essential part of large hospitals. Today we have the principle of the combined investigation of the patient by a group of specialists accustomed to work together. This is one of the inevitable results of specialism and it will grow not only within our hospitals but with the growth and expansion of diagnostic and treatment centers and with group practice.

I submit, once again, that the quality of medical care rests upon the quality of medical education as related to research. The organization and endowment of medical research, the establishment of institutes for scientific research, and the multiplication of opportunities to advance knowledge and specialize has enabled large numbers of young men who otherwise could not afford to give their whole time to research and teaching, to do so without distracting anxiety. Today, more than ever before, generous endowments and fluid funds have been made available by the public, either through voluntary giving or by means of tax funds, so that opportunities for original work have greatly increased. Formerly, researches advancing medical knowledge and medical practice were largely due to individual and isolated effort but now teamwork and group enterprise has become more general and prolific. As the late Francis Blake remarked when he was President of the Association of American Physicians, the big change in medical communication in the past 50 years has been in the production of research and writing by multiple authorship rather than by individuals.

Medical education throughout its entire range—undergraduate, graduate and postgraduate—is attracting widespread attention and most serious consideration and, as a result, revolutionary changes are under way. Much modification, organization and improvement have followed. New groups have accepted new responsibilities and new and important observations are being made in steadily increasing numbers. The proper sifting, and the proper incorporation of this new knowledge into medicine will lead to large profits for medical science and its practice.

About 50 years ago, storm warnings and complaints about the dangers of specialization were being raised but, in spite of these protests, this was only the beginning. Between 1917 and 1950, the American Medical Association recognized 19 specialties but these 19 are by no means all because medicine's domain has been further divided and subdivided so that there are today at least 50 medical specialties and as many if not more medical aids. It has been said that the specialists crowd about the patient, each proffering his skilled services with eagerness, a whole company of men to care for the stricken corporal or even the stricken general! There are some who say perhaps they should stand back to give the sufferer air; at least they should withdraw a bit to relieve the patient's bewilderment and to give him some perspective for a choice. But there are more to come, because, as knowledge advances, new specialties will be born. They will be developed by the young, the imaginative and the curious. They will be developed by our youth who have the imagination and the energy to keep knowledge alive and by those who are dedicated to seeking the truth and advancing knowledge for the benefit of mankind and the general welfare.

In your own specialty of gastroenterology, the advances which have been made in diagnosis and in treatment in the past 50 years are almost incredible. The problems awaiting solution are numerous and complex. They challenge the

imagination and call for intensive investigation. While difficult and urgent, the rewards in terms of alleviating human suffering are high.

Your College, which is a body of colleagues with common interests, functions and privileges, will need to continue to extend and improve, stimulate and encourage research and education in the highly important field of gastroenterology. No field of science can be neglected—physics, chemistry, biology, atomic energy, all viewed in biological perspective, must be emphasized and pursued with vigor. All of the sciences need support and especially our medical institutions that stress research and education in the natural and biological sciences. Advances in the medical sciences flow from advances in the biological sciences and your band of colleagues must take the lead in promoting and supporting research and education in your chosen specialty. Institutions of learning and young men need your encouragement and support.

In the autumn of 1926, Professor Starling told the London Physiological Society how he and Professor Bayliss discovered the two-fold character of intestinal peristalsis which they referred to as the law of the intestine. They had been invited by Sharpey-Shaffer to contribute an article on the physiology of the intestine for his textbook. They started by examining the literature but soon discovered that practically nothing was known about complex movements of the intestine, so, like true scientists, they set to work, designed some experiments and discovered that the advancing wave of constriction was preceded by an area of inhibition or relaxation so that peristaltic movement consisted of two parts, following in definite sequence and combining to facilitate the onward or downstream movement of the intestinal contents. Thus when they were confronted with the problem of writing something about a subject about which nothing of substance was known, it was necessary for them to find out how the intestine moved. They had to resort to the experimental method. In your specialty, like all specialties founded upon science rather than empiricism, it is necessary to ask the question and seek the answer by the experimental method.

Specialties are born by a desire on the part of men to learn more and more about a subject as an intellectual pursuit. That is the true motivation of all specialties. The people benefit because specialists are applying their knowledge for the alleviation of human suffering.

In the days ahead, specialism of all kinds will increase and your specialty will broaden and deepen. More and more young men will be seeking the rating of a specialist, more and more young men will want to cross your specialty with the specialty of others. Also your specialty will change and the best young men will start using concepts and terminology you will not be able to understand though you know you ought to be able to do so. All of these changes are a part of the natural history of a specialist as well as a specialty, and the specialist must be prepared emotionally for each stage. In order to further your specialty

in the days ahead, it will be necessary to preserve the imagination of youth, to encourage the cross-fertilization of all the disciplines in science and to avoid anger and resentment when your specialty is attacked, ignored or belittled. I warn you not to fall into the trap of believing that your specialty is not attracting the able youngsters that used to go into it, because this is not true. Just remember that, as science advances, new conditions are created and specialties and specialists change, and we change with them.

So, in the years ahead, specialties and specialists will both increase and change. Prepare thyself for change and adapt and adjust to the change with dignity and grace and without embitterment, loneliness or wonder.

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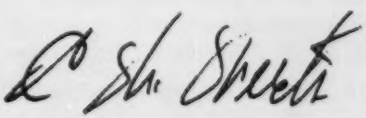
President's Message

Motivation

In a report in *Science,* 20 December 1957, by Neal E. Miller important objective data collected from a series of excellent experiments shows that animals can be motivated by learning to avoid painful experiences or by obtaining desirable rewards. In normal animals the degree of motivation determined the accomplishment. It is generally agreed that this is true of man also.

The development of a stimulus of this nature for our membership undoubtedly was inherent in the recommendations of the Committee on Postgraduate Education when they suggested a modification in the requirements for members to advance to Associate Fellowship. This suggestion was approved by the Board of Trustees and now appears in the revised Constitution and By-laws, copies of which are being mailed to all members. This modification provides that "a member, in lieu of Board eligibility, may be advanced to Associate Fellowship provided that he has successfully completed the prescribed number of hours in Postgraduate courses approved by the Committee on Postgraduate Education of the College. The number of hours required for advancement shall be determined from time to time by the Board of Trustees". (The present requirement is 50 hours).

This opportunity for advancement in the organization should be sufficient to motivate every member to attend our postgraduate courses. Apart from this motive, however, the excellence of the course given in Boston in 1957 and the one planned for the New Orleans meeting next October makes the solid educational value of these courses such that few members will willingly miss them.



EDITORIAL

Carbon Monoxide Poisoning (Coma)

With the advent of the Winter many cases of carbon monoxide poisoning will occur due to gas heaters and coal burning stoves. The physician who is called to see a patient is confronted with determining the possible cause of the condition; whether the coma is due to uremia, diabetes, food or other poisoning. In all doubtful cases, if possible, it is advisable to ascertain the cause and act quickly to revive the patient.

The diagnosis of nonfatal carbon monoxide poisoning is baffling in the absence of a definite history of exposure to the gas. With large concentrations of carboxyhemoglobin the skin may show a pinkish flush, but this is not always apparent in the living patient as it is in an ecchymosis or bruise of the dead body. Carbon monoxide poisoning, however, should be suspected in obscure cases of coma attended by marked spasticity of the extremities and the presence of hyperactive and abnormal deep reflexes, clonus and signs suggesting bilateral involvement of the pyramidal tracts.

For a definite diagnosis it is advisable to withdraw blood for qualitative chemical examination for determining the presence of carboxyhemoglobin. A rapid and simple qualitative test may be done on 2 or 3 c.c. of blood by diluting it and then adding a few drops of 10 per cent sodium hydroxide solution. A light pink color will result and persist after addition of the alkali. Normal blood in the same dilution will turn a greenish brown on addition of the alkali. A qualitative test as well as a spectroscopic test will give a positive result only if the concentration of carboxyhemoglobin in the blood is more than 10 per cent.

The important thing to remember in a nonfatal case is to examine the blood as soon as possible, since carbon monoxide is rapidly eliminated from the blood after a person who has been exposed to it has been removed from the environment of the gas and allowed to breathe fresh air. The elimination of the poison occurs even more rapidly if respirations are stimulated and oxygen administered. In fresh air, about half the monoxide in the system will be eliminated during the first hour of survival. After 24 hours, all the carbon monoxide will have disappeared. Thus in a case after survival it may be difficult to prove that carbon monoxide poisoning actually was the cause of the coma.

The prognosis in acute carbon monoxide poisoning depends on immediate removal of the patient to fresh air, administration of artificial respiration, oxygen or a mixture of 7 per cent carbon dioxide and 93 per cent oxygen. Many persons who are found unconscious survive for 24 hours and even longer. They may regain consciousness only to lose it again or they remain comatose until they die, as a rule of hypostatic bronchopneumonia.

To administer drugs hypodermically to stimulate respiration is a doubtful question. The only drug that may be indicated is caffeine as a respiratory stimulant.

Samuel Weiss, M.D., F.A.C.G.

ABSTRACTS FOR GASTROENTEROLOGISTS

ESOPHAGUS

RUPTURE OF THE ESOPHAGUS: Harold L. Bushey. New England J. Med., 255:146 (13 Dec.), 1956.

The etiology of rupture of the esophagus may be divided into 3 groups: 1. instrumentation and foreign body 2. neoplasma or long-standing local disease as for instance chronic esophagitis 3. spontaneous. The cases of this so-called spontaneous group present the greatest diagnostic difficulties. The clinical symptoms suggesting rupture of esophagus are: vomiting, severe pain in left chest or left upper abdomen, dyspnea, prostration of patient, subcutaneous or mediastinal emphysema hydropneumothorax. The author presents 2 interesting case histories and discusses the diagnostic difficulties as well as timing and methods of surgery.

H. J. Joseph

PEPTIC ESOPHAGITIS, MARGINAL ULCERATION, AND PEPTIC ULCER OF THE ESOPHAGUS: Asher Winkelstein. Am. J. Digest. Dis., 2:7 (Jan.), 1957

This paper is a discussion of the three abnormal esophageal conditions under the three headings. The author reviews the names that historically have been associated with these conditions.

He states that *peptic esophagitis* may be associated with duodenal ulcer, intubation, vomiting, anastomotic operations, idiopathic, and rarely with hiatus herniae. Its characteristics are long, tubular; exudate, ulceration; stenosis, hemorrhage; secondary small herniae; medical therapy, good response.

Marginal peptic ulceration may be associated with sliding hiatus herniae and small herniae (infantile?, congenital?). Its characteristics show a short stretch "marginal" ulceration; superficial; stenosis; frequent dilations necessary; usually in gastric mucosa; often surgical.

Solitary *peptic ulcer of the esophagus* shows persistent embryonal columnar epithelium in lower esophagus. Its characteristics are that it penetrates, perforates; hemorrhage; small herniae associated; often surgical.

I. H. Einsel

STOMACH

BAD GASTRECTOMIES: V. J. Kinsella. Brit. M. J. 5004:1277 (1 Dec.), 1956.

There are differences of opinion concerning the late results of partial gastrectomy for peptic ulcer. A survey of the literature confirms the opinion of Ogilvie that "the bad results of gastrectomy are the results of bad gastrectomy". The commonest fault in technic is an improper placement of the afferent loop, which results in the so-called "dumping syndrome", and the proper placement is described.

Substitute operations aimed at conserving ulcer-prone tissue are based on an inadequate conception of the pathology of ulcer and will result in an excessive number of recurrences and other complications. Operations which include replacement of the stomach by isolated loops of bowel are unnecessary and should therefore be abandoned.

In gastric surgery, bad results and confusion reign today because insufficient attention has been paid to the old masters who fashioned the operation. Gastric surgery should only be performed by those surgeons who have received special training, as gastrectomy involves a more extensive and delicate reconstruction than that required in most major operations.

ARNOLD L. BERGER

BILLROTH I RESECTION: Milton W. Durham. Northwest Med. 55:1361 (Dec.), 1956.

The author feels that subtotal gastric resection is the best available operative treatment of peptic ulcer, the Billroth I anastomosis providing certain advantages over the Billroth II procedure. These advantages are listed as follows:

1. It is technically easier and quicker, with less anesthesia time.
2. It is advantageous in gastric ulcer and for palliative gastric resection for carcinoma because of the mobility of the duodenal stump, which simplifies the anastomosis.
3. It is particularly advantageous in cases of jejunal ulcer and of severe physiologic distress occasionally following the Billroth II.
4. Recurrent ulceration is no greater and perhaps less than after other operations.
5. The dumping syndrome has been less severe and of shorter duration than with other types of anastomosis.
6. Weight gain has been greater and more rapid, probably due to better physiologic mixing of food and less postoperative disturbance.
7. Economic rehabilitation has been more complete and more rapidly achieved than with the Billroth II.

JOHN E. COX

PANCREATOSPLENECTOMY OR HEPATECTOMY COMBINED WITH GASTRECTOMY IN THE TREATMENT OF CARCINOMA OF THE STOMACH: Komei Nakayama. J. Internat. Coll. Surgeons 26:651 (Dec.), 1956.

The author presents his studied data on 39 cases of gastric malignancy. He advocates a gastrectomy combined with pancreatosplenectomy or hepatectomy for cancer of the stomach in selected cases. In addition to the clinically observed cases he presents a tabulation of experimental data. Emphasis is placed throughout this report on the author's method for transection of the pancreas as well as resection of the left lobe of the liver. The author advocates this operative procedure in selected cases with gastric malignancy.

BERNARD J. FICARRA

A CLINICAL EVALUATION OF TUBELESS GASTRIC ANALYSIS: Robert J. Bolt, Theodore G. Ossius, and H. Marvin Pollard, Gastroenterology 32:34 (Jan.), 1957.

The azure A cation exchange resin test for the presence of free hydrochloric acid is an extremely simple test applicable to surveys of large groups of individuals. The authors found an accuracy of 97.7 per cent in 369 of 378 individuals tested for free acid, and 97.0 per cent accuracy in 128 of 132 patients with achlorhydria. Sensitivity to the drug is rare with only one mild reaction occurring in their series.

SAMUEL M. GILBERT

INTESTINES

MASSIVE INTRAPERITONEAL HEMORRHAGE FROM APPENDIX EPIPLOICA: Leon H. Manheimer. New England J. Med. 255:570 (20 Sept.), 1956.

The appendix epiploica frequently requires surgery for infarction following torsion of the appendix on its long axis. Here is reported, probably, the first case of intraperitoneal hemorrhage from this appendage.

A 58-year old male developed symptoms suggesting appendicitis, but with no nausea or vomiting, and was taken to surgery with this diagnosis.

Blood welled from the opened peritoneum and the diagnosis was changed to ruptured spleen, when the liver was found on exploration to be intact.

However, when a costal incision revealed a normal spleen with no blood in the upper abdominal cavity, a search uncovered a large appendix epiploica arising from mid sigmoid and pointing across the rim of the pelvis, with a hematoma at its distal end and blood oozing from a break in its peritoneal covering, and at its base a small tear from which a tiny arteriole was pumping blood.

The entire fatty specimen was removed and pathologic examination showed "recent hemorrhage into fatty tissue, with early focal fat necrosis and focal acute vasculitis, (nonspecific)."

J. Edward Brown

ASSOCIATION OF SALMONELLA ENTERITIS WITH OPERATIONS ON THE STOMACH: William R. Waddell and Lawrence J. Kunz. New England J. Med. 255:555 (20 Sept.), 1956.

Diarrhea following operations for gastric or duodenal ulcer has been attributed to the mechanical interference of the surgical procedure.

Nine cases have been reported in the past two years due to salmonella infection, and from these samplings it may be deduced that poor results following gastric surgery may be traceable to acute or chronic infection by this organism.

It may be that abnormal gastric physiology following surgery enhances susceptibility to this infection well beyond that under normal functioning, where the acid content of stomach is low or lacking and the rapid passage of food into the intestines allows quicker egress of the salmonella into the colon.

J. Edward Brown

THE TREATMENT OF INTESTINAL PARASITIC INFECTIONS: R. C. Jung and E. C. Faust. A.M.A. Arch. Int. Med. 98:495, 1956.

The authors recommend the following medications: *Amebiasis*: Erythromycin 0.5 gm. q. 8 hrs. for 7 days. This alters the intestinal flora less than the tetracyclines. Antibiotics should be combined with Milibis 0.5 gm. t.i.d. for 8 days, of Diodoquin grains x, t.i.d., for 21 days, or Fumidal 10-20 mg. t.i.d. for 7 days. Also in all cases of intestinal amebiasis chloroquine should be added, the dose is 0.5 gm. twice daily for 2 days, then 0.25 gm. twice daily for 21 days. *Refractory amebiasis:* watch for coexisting other intestinal disease, nutritional deficiencies, contaminated food or water, or other sources of reinfection. Ameboma responds only to emetine, it may be coexisting with carcinoma. Amebiasis due to amebae other than histolytica responds to the same drugs.

Balantidiasis: Human infection originates either from pigs or infected humans. Best therapy: Terramycin 1.5 to 2.0 gm. daily for 10 days.

Trichinosis: During early stage give Piperazine Citrate 2-3 gm. daily for 7 days.

Trichuriasis: Best available therapy, Hexylresorcinol retention enemas, 0.2 per cent, 400-500 c.c., followed after 30 minutes by a tap water enema, must be repeated. In tropical America Leche de higueron, single oral dose of 60 c.c. of fresh unpreserved sap of this tropical fig tree. In all cases, Ferric and Ammonium citrate, 6 to 12 gm. daily for several weeks is a useful agent.

Schistosomiasis Mansoni, seen in Puerto Ricans: Antimony potassium tartrate 0.5

per cent I.V. solution in dextrose water or saline for adults. Start with 8 c.c., increase by 4 c.c. until 28 c.c. are reached, give on alternate days a total of 18 injections. For children, Fuadin, i.m., is preferred.

H. B. EISENSTADT

VOLVULUS OF THE SPLENIC FLEXURE: Maxwell H. Poppel, Bertram E. Zeitel and Raymond M. Abrams. Am. J. Digest. Dis. 1:380-386 (Sept.), 1956.

Volvulus of the splenic flexure is an unusual type of large bowel obstruction. The authors found only one operative case reported in the literature. To this they add two more proved cases and discuss their etiology. In the first case, a very rare congenital absence of the greater omentum and peritoneal attachments of the flexures predisposed to volvulus of the splenic flexure. In the second case, a short mesocolon at the splenic flexure together with a chronic, benign obstruction in the sigmoid allowed for progressive dilatation of the splenic flexure and twist. A splenic flexure with normal peritoneal attachments in the absence of distal pathology would not usually undergo volvulus.

WALTER CANE

MEGACOLON: TREATMENT BY RECTOSIGMOIDECTOMY: Daher E. Cutait. J. Internat. Coll. Surgeons 26:485 (Oct.), 1956.

Two theories exist to explain the pathogenesis of acquired megacolon. First achalasia of the pelvic-rectal sphincter. The dilatation of the sigmoid is due to the lack of relaxation of the rectopelvic sphincter caused by an inflammatory lesion of Auerbach's plexus. The method of operation would be abdominal rectosigmoidectomy.

If one considers dyskinesia of the distal portion of the intestine as the cause of acquired megacolon, one would consider abdominalperineal rectosigmoidectomy as the operation of choice.

The results of 200 cases—operations performed from May 1947-April 1956 are analyzed.

The author believes in the theory of dyskinesia, as—in his opinion—there is no sphincter in the rectopelvic region.

The most possible and frequent postoperative complications are: cystitis and partial disruption of the anastomosis with and without sinus-tract formations. After abdominoperineal rectosigmoidectomy serious sexual troubles—namely *impotentia coeundi*—were observed. This sexual incompetence may be caused by a lesion to the erector nerve during dissection of the rectum. Consequently only in the younger male patient the author prefers to do the abdominal rectosigmoidectomy.

H. J. JOSEPH

RECURRENT HERNIAE: Alfred H. Iason. J. Internat. Coll. Surgeons 26:409 (Oct.), 1956.

The author lists the causes of recurrent herniae as follows: 1. Preoperative causes regarding the planning of the primary operation, consisting of both surgical and medical errors in judgment. 2. Sixteen different so-called surgical causes regarding the procedures at the primary operation and 3. Five postoperative causes, namely persistent coughing, lifting of heavy weights, straining at bowel-movements, severe manual efforts before a minimum of three months after operation and prostatic obstruction.

The anatomical varieties of recurrent herniae are summarized.

The anatomical backgrounds and the myodynamics of genesis of hernia are explained in detail.

The author stresses the necessity of profound knowledge of anatomy by the surgeon and the implications of congenital and abnormal defects.

In selecting the type of operation and repair the surgeon should keep in mind the pathology before operation and possible pathological changes caused by surgery.

The standard surgical procedures are explained in minute detail.

The author stresses the logical conclusion, that primary repair of hernia has to be individualized. This individualization is still more important at repair of recurrent her-

nia. The additional use of tantalum has proven valuable in selected cases.

This article and its colored illustrations are of such outstanding value, that a short summary cannot do it full justice.

H. J. JOSEPH

STAPHYLOCOCCAL GASTROENTERITIS, REPORT OF A MAJOR OUTBREAK: Harry Wain and Paul A. Blackstone. Am. J. Digest. Dis. 1:424-429 (Oct.), 1956.

The authors, members of the Department of Health, Mansfield, Ohio, give a vivid account of a major outbreak of food poisoning which assumed the proportions of a community disaster. It caused the acute illness of 244 out of 306 individuals attending a picnic on a hot day, at which ham was served that had been sliced by a man who subsequently was found to have three open acne lesions discharging pus. The authors emphasize that the characteristic feature of staphylococcal gastroenteritis is the relatively short incubation period, which is usually 1 to 6 hours while that of botulism and of salmonella enteritis range between 12 and 24 hours. If the incubation period is longer than 11 hours, staphylococcal enteritis can be ruled out. Fatal outcome is extremely rare, and recovery is complete within 24 hours, with or without symptomatic treatment. The three foods most often responsible in order of frequency are meat products, especially ham, cream and custard bakery products, and poultry.

WALTER CANE

PERFORATION OF THE COLON DURING A BARIUM ENEMA STUDY, DEVELOPMENT OF RETROPERITONEAL, MEDIASTINAL, AND CERVICAL EMPHYSEMA: Jerome H. Shapiro and Harold Rifkin. Am. J. Digest. Dis. 1:430-435 (Oct.), 1956.

MASSIVE PNEUMOPERITONEUM AND PNEUMORETROPERITONEUM AFTER GASTROSCOPY: David Katz and Sydney Selesnick. Am. J. Digest. Dis. 1:512-520 (Dec.), 1956.

The two case reports may serve as reminders that, though extremely rare, such mishaps do occur. The prognosis is fortunately favorable, and the treatment is conservative.

Excellent x-ray pictures accompany both case reports.

WALTER CANE

PROCTOLOGY: E. Parker Hayden. New England J. Med. 255:809 (25 Oct.), 1956.

This report presents the latest methods of managing various lesions of the lower bowel. The discussion presents a method of managing hemorrhoids which in the majority of instances fall into the accepted pattern. The paragraphs treating of intestinal antisepsis postulates the superiority by some authors for the use of neomycin. The paragraphs on pseudomembranous ulcerative colitis recall to mind the existence of this entity in certain patients. The use of Dicrysticin is mentioned and this is a suggestion worthy of note since it has proven to be quite efficacious in the therapy of this disease. The notation on anorectal sepsis in leukemia is a point well taken. Attention is called to the fact that an ulcerating anorectal disease may be the result of an underlying leukemia. Under the heading of ulcerative colitis the advocacy of abdominoperineal resection plus colectomy in certain patients is substantiated.

BERNARD J. FICARRA

PROCTOLOGY (CONCLUDED): E. Parker Hayden: New England J. Med. 255:854 (1 Nov.), 1956.

The concluding remarks on this survey on proctology presents the current theories on the origin of pilonidal sinus. More valuable is the discussion on diverticulosis and diverticulitis. The salient point under this heading is the fact that hemorrhage may

be the only visible sign of this serious disease process. The paragraphs on spontaneous perforation of the colon is especially worthy of note since many physicians and surgeons are in doubt that this can occur. The problem of adenoma (mucous polyps) is again evaluated and the surgical extirpation of these polyps is still an advocated procedure. Familial multiple polyposis is discussed and the treatment here is again surgery. The syndrome of Peutz-Jeghers is mentioned. This consists of melanotic spots on the lips in association with gastrointestinal polyps. The importance of the pigmented spots resides in the fact that such patients should have an examination for polyps. The cancer question is again reiterated with early diagnosis and treatment as the *sine qua non* of better prognosis.

BERNARD J. FICARRA

DIVERTICULOSIS AND DIVERTICULITIS OF THE COLON: Arthur W. Allen and Glenn E. Behringer. Pennsylvania M. J. 59:1345 (Nov.), 1956.

Diverticulosis is a disease of full adult life that appears with increasing frequency as age develops. At the age of 85 approximately two-thirds of such patients will be so affected. About two-thirds of these patients have minimal or no symptoms. The remaining one-third have diverticulitis of sufficient magnitude to warrant or demand surgical treatment. This is based on 210 consecutive patients treated by resection in the Massachusetts General Hospital since 1942. The younger the patient with this disease, the more logical radical treatment becomes. Their life expectancy is long, and if left untreated, one of the serious complications will develop. These are urinary fistula, abscess, or frequent bouts of acute inflammation. Most of the patients in this age group can have a one-stage operation if so treated as soon as urinary symptoms occur or severe inflammation takes place. Many people with long-standing diverticulitis become chronically obstructed. They can be safely relieved of this distressing malady by a well-planned resection, usually at a time of election.

JACOB A. RIESE

BOWEL OBSTRUCTION, UNUSUAL MANIFESTATION OF WEBER-CHRISTIAN DISEASE: Marvin E. Sattler and A. I. Greenberg. Wisconsin M. J. 55:1219 (Nov.), 1956.

Weber-Christian disease is predominantly a skin disorder characterized by recurrent, tender or nontender, subcutaneous nodules consisting of granulomatous infiltration of the fat tissue with fat necrosis. However, various visceral organs may be involved by the same pathological process such as the heart, the liver, the spleen, the pancreas, the kidneys, and the adrenal glands. In addition, perivisceral panniculitis produces a chronic adhesive peritonitis which might lead to obstruction. An unusual case of panniculitis with such sequence of events is reported. The patient manifested hepatomegaly, polyarthritis, fever, anemia and leukopenia and a necrotizing hemorrhagic ulcerative enterocolitis with nausea, vomiting, diarrhea, melena and weight loss. Finally, intestinal obstruction occurred requiring laparotomy and resection of 44 inches of terminal ileum. These events preceded the skin eruption by several weeks. Weber-Christian disease with wide-spread visceral involvement resembles the various collagen disorders.

H. B. EISENSTADT

MASSIVE COMPOUND INTUSSUSCEPTION: Robert E. Mullarkey. Northwest Med. 55:1215 (Nov.), 1956.

Intussusception usually involves the distal small bowel or terminal ileum and proximal colon. There are four cardinal symptoms: periodic attacks of pain, vomiting, passage of blood by rectum, and the presence of a palpable tumor in the abdomen. Digital examination of the rectum when combined with palpation of the abdomen may disclose a mass not otherwise felt. The author reports a case of massive

compound intussusception in a three-year old child with a double ileoileal intussusception involving a Meckel's diverticulum (first an intussusception of Meckel's diverticulum into the small bowel and secondary intussusception of the small bowel with the diverticulum into the lower level of the small bowel). Compound intussusception is rare, there is more vomiting and bleeding and the prognosis is worse due to delay in diagnosis and treatment.

ARNOLD STANTON

LYMPHOBLASTOMA (LYMPHOSARCOMA) OF THE PERITONEUM AND INTESTINE: Walter W. Ebeling. Northwest Med. 55:1210 (Nov.), 1956.

The author reports two cases of abdominal lymphoblastoma. The first was a woman of 64 years with a pelvic tumor which turned out to be a lymphosarcoma (follicular lymphoma). The second was a woman aged 73 who presented with ascites and weight loss and in whom biopsy revealed reticulum cell sarcoma. She did well following irradiation but later developed an annular obstructing lesion in the descending colon. Best results were obtained by surgery as early as possible followed by irradiation repeated as often as necessary.

ARNOLD STANTON

NONTROPICAL SPRUE: Mandred W. Comfort and Earl G. Schulz. A.M.A. Arch. Int. Med. 98:807, 1956.

Nontropical sprue is a bowel dysfunction producing impairment of absorption not only of fat, but also of protein, carbohydrates, vitamins, minerals and even water. This defective absorption causes diarrhea, weight-loss in spite of good appetite, hypoproteinemia, ascites, osteomalacia, tetany, hypocalcemia, hyponatremia, hypokalemia, hypolipemia, iron and Vitamin B_{12} and folic acid deficiency, anemia, glossitis, stomatitis, cheilitis, skin lesions of pellagra, Vitamin D deficiency with hypoprothrombinemia, and nocturia. The latter is due to prolonged retention of water in the intestines after ingestion. Diagnosis is confirmed by the presence of large, bulky stools with excessive fat, by a flat oral glucose and Vitamin A tolerance curve, and a small bowel x-ray picture revealing altered mucosal relief, hypomotility, hypersecretion and fluid retention.

Differential diagnosis must include: 1. steatorrhea of chronic pancreatitis with history of recurrent abdominal colics, diabetes, calcifications, responding to pancreatic therapy, 2. steatorrhea of pancreatic cancer, a rare disorder with fast progression and fatal outcome, 3. fibrocystic disease in adults with familial appearance and chronic pulmonary disorders, 4. regional ileitis, enteroenteric fistulas, long standing partial bowel obstruction, short-circuit bowel, and various other abnormal states following stomach and bowel surgery. All those disorders have an abnormal x-ray finding, 5. Whipple's disease with pigmentation, arthritis, pleural and pericardial effusions, abdominal masses and positive lymph node biopsy, 6. diabetic neuropathy with intractable diarrhea resistant to any form of treatment, 7. amyloidosis and scleroderma with involvement of skin and various viscera, 8. lymphosarcoma and other malignant tumors of the small bowels with fast progression and fatal termination within less than 3 years, 9. tropical sprue. The latter might be identical with the nontropical variety but is usually distinguished by seasonal incidents, occurrence in certain tropical regions, affecting many inhabitants at the same time, developing abruptly and running a fast course, showing macrocytic anemia with megaloblastic bone marrow, hardly ever leading to osteomalacia and tetany, occurring in persons with deficient ingestion of food, particularly protein, being completely curable by liver extract, folic acid and Vitamin B_{12}.

Treatment of nontropical sprue requires physical and mental rest, a diet high in protein, high in carbohydrates derived from fruits and simple sugars, high in Vitamins A, D, B-complex, B_{12}, K, calcium, potassium, iron, folic acid, and low in fat and gluten containing flours. Blood transfusions may help resistant anemia, infusions of human serum albumin Vitamin D resistant tetany. Cortisone and corticotrophin have a beneficial effect during acute relapse.

H. B. EISENSTADT

SEVERE OSTEOMALACIA ASSOCIATED WITH OCCULT STEATORRHEA DUE TO NONTROPICAL SPRUE: John L. Juergens, Donald A. Scholz and Eric E. Wollaeger. A.M.A. Arch. Int. Med. 98:774, 1956.

The most frequent cause of osteomalacia in the United States is prolonged intestinal disease, especially nontropical sprue.

Diagnosis of osteomalacia is based upon the finding of a low serum calcium, a normal or low serum phosphorus and usually an increased alkaline phosphatase. There is also a demineralization of the skeleton, codfish vertebrae, true fractures and particularly symmetrical pseudofractures, the latter are situated on the femoral necks, the pubic and ischial bones, the ribs and the scapula. There will be also symptoms of tetany. Diagnosis of nontropical sprue requires a careful history in regard to past diarrhea and other bowel dysfunction, bulky and fatty stools, weight loss, and a deficiency pattern on the x-ray film. Treatment consists, apart from high protein, high carbohydrate and low fat diet, of Vitamin D 50 to 300,000 units daily and calcium lactate powder 3 to 9 teaspoonfuls daily dissolved in hot water and ingested after cooling.

H. B. EISENSTADT

BACTERIUM COLI 0.125;B15 IN INFANTILE GASTROENTERITIS: William McNaught. Scottish M. J. 1:376 (Dec.), 1956.

Since 1945, Bacterium Coli 0.111;B4, 0.55;B5, 0.26;B6 and 0.87;B7 have been recognized as the causative organisms of infantile gastroenteritis, but in 1952, B. Coli Canioni, (0.125;B15) was encountered as the offending agent in 60 children who showed diarrhea or deranged stools, exhibiting however, but 30 per cent morbidity, in comparison with 70 per cent morbidity of those infected with B4, B5 and B6 and only 5 per cent severe diarrhea.

An interesting finding was that of 13 infants only one harbored 0.125;B15 on admission and the other 12 picked up the organism after admission, of these 3 developed gastrointestinal symptoms but not of a severe type.

B. Coli 0.125;B15, a nonmotile, nonflagellated rod was present in profuse numbers from samplings of ward dust.

As most of the children studied were premature or under one year of age, it may be that 0.125;B15 attacks at this age more frequently than at an older one.

In view of finding that 74 per cent of those cross infected in the wards remained symptom-free, the morbidity of 0.125;B15 in general infant population is probably very small.

J. EDWARD BROWN

WHAT IS NEW IN THE TREATMENT OF ULCERATIVE COLITIS?: David J. Sandweiss and Marcus H. Sugarman. J. Michigan M. Soc. 55:1461 (Dec.), 1956.

Definite medical and surgical advances in recent years permit the majority of patients with ulcerative colitis to be treated satisfactorily. Azulfidine orally, the steroids and newer feeding technics permit 80 per cent of these patients to avoid surgery. The latter is reserved for the 20 per cent that respond poorly to a medical regimen. Usually then a colectomy or ileostomy will be done and a mortality rate of as low as 2 per cent has been reported.

The current enthusiasm for prophylactic surgery in long standing cases to prevent the occurrence of carcinoma or other complications is attacked since the incidence of these is no higher than the usual surgical mortality.

Nevertheless, the author lists 8 indications for surgery, for in these cases surgery offers the only favorable results in our present state of knowledge. These indications are as follows:

1. Acute fulminating colitis not responding to adequate medical therapy 2. perforation 3. rectal and colonic stricture and obstruction 4. extensive perirectal infection and fistulas 5. carcinoma or defect suspected of being carcinoma 6. profuse hemorrhage or repeated severe hemorrhages 7. extensive secondary polyposis 8. semi-invalidism.

A. M. SUSINNO

PREVENTION OF POSTOPERATIVE PAIN IN RECTAL SURGERY: Eugene Laurisin. J. Michigan M. Soc. 55:1479 (Dec.), 1956.

"Postoperative pain following anorectal operations has always been considerably greater and more prolonged than pain after other operations." This statement is still valid today despite the contributions of improved surgical technics. Hence the author advises local aseptic anesthesia in addition to whatever general anesthesia is used for anorectal surgery.

Either the water soluble or the oil soluble preparations are advised provided the differences in technics and results of each are appreciated.

Although more than half of all rectal carcinomas can be diagnosed by digital examination, sigmoidoscopy is urged as part of all routine examinations. In the author's opinion the majority of proctologic problems can be diagnosed and treated by the generalist.

A. M. Susinno

PSEUDOMEMBRANEOUS COLITIS COMPLICATING PROLONGED ANTIBIOTIC THERAPY: Henrick A. Hartmann and D. Murray Angevine. Am. J. M. Sc. 232:667-673 (Dec.), 1956.

Seventeen cases of pseudomembraneous colitis diagnosed postmortem are reported. These represent 1 per cent of all necropsies performed in a four-year period. All of these patients had received antibiotics. Some had received more than one antibiotic and all had received antibiotics over a long period of time. The authors postulate that changes in the intestinal bacteria flora may occur with a reduction of the E. coli and other vitamin synthesizing microorganisms with the resulting growth of vitamin-requiring microorganisms, among them staphylococcus aureus and proteus vulgaris. It is thus felt that pseudomembraneous colitis may be a vitamin deficiency manifestation. Pantothenic acid is the vitamin felt by the authors to be involved. A review of literature and a review of experimental facts in animals is included to help strengthen the arguments for this concept.

Bernard Farfel

PRIMARY PERFORATED JEJUNAL ULCER: Bernard P. Strouth and John A. Edwards. Northwest Med. 55:1359 (Dec.), 1956.

Primary perforated jejunal ulcer is a rare cause of peritonitis, up to this time about fifty cases have been reported. There is no definite diagnostic procedure unless the lesion is detected incidentally by the roentgenologist in a routine search for ulcer of the upper intestinal tract. One case of jejunal ulcer with perforation is reported in an 83-year old female. A perforation was found about 8 inches from the ligament of Treitz. A primary resection was done with uneventful recovery.

This case differs from the majority in that the perforation was on the mesenteric border, thus requiring resection.

It is felt that five-hour pictures following the administration of barium may be instrumental in detecting more of these lesions.

John E. Cox

ACUTE MANSON'S SCHISTOSOMIASIS: R. S. Diaz-Rivera, F. Ramos-Morales, E. Koppisch, M. R. Garcia-Palmieri, A. A. Cintron-Rivera, E. J. Marchand, O. Gonzales and M. V. Torregrosa. Am. J. Med. 21:918 (Dec.), 1956.

The authors, a group from the University of Puerto Rico School of Medicine, have reported 12 cases of acute Manson's schistosomiasis studied in Puerto Rico during the past six years. The disease is the self-limited phase of infection which follows the first or several consecutive exposures to the cercariae of S. mansoni. This is characterized by a variable asymptomatic incubation period, infrequent early cutaneous manifestations, and an explosive onset with severe constitutional manifestations indistinguishable from those of an acute infectious disease such as typhoid fever, and symptoms and signs dominated by gastrointestinal, hepatic and pulmonary dysfunc-

tion. The clinical picture is dominated by a severe hypersensitivity state, the adult parasites and their eggs being the sources of allergens. The severity of the disease depends on the extent of organ hypersensitivity. Liver function tests such as the cephalin flocculation, thymol turbidity, and bromsulfalein, are frequently if not invariably altered in the disease. Hyperglobulinemia with increased gamma fraction is invariably present together with hepatomegaly, splenomegaly and generalized lymphadenopathy. Serial biopsy specimens of the liver studied from 62 to 18 months after infection demonstrate an early and diffuse eosinophilic infiltration and pseudotubercle formation. Whether other factors such as chronic debilitating diseases and nutritional deficiencies play a part in the pathogenesis of hepatic cirrhosis in Manson's schistosomiasis remains to be determined. The clinical alterations attributed to the hypersensitivity state are unaltered by treatment. Early treatment leads to improvement in the severe lassitude and anorexia with rapid weight increase. It fails to prevent focal lesions in the liver and large intestine or to shorten the febrile course. Courses in fuadin may be effective in suppressing oviposition for as long as five months to one year but fail to eradicate the parasites.

JOHN M. MCMAHON

CHRONIC OBSTRUCTING ILEITIS TREATED WITH A SIMPLE ILEOCOLOSTOMY: Edwin J. Grace. Med. Times 84:1299 (Dec.), 1956.

A case of chronic obstructing ileitis with a 26-year follow-up is reported. In April, 1930, a simple ileocolostomy was performed for partial obstruction of the terminal ileum. In June 1956, after complete laboratory and x-ray studies, the patient was found to be in excellent condition. The review of this case, after 26 years, was presented to show agreement with the opinions of the conservative surgical-medical team who treated President Eisenhower, to lend support to the optimistic prognosis, which seems justifiable and warranted.

ARNOLD L. BERGER

TREATMENT OF ULCERATIVE COLITIS WITH LOCAL HYDROCORTISONE: S. C. Truelove. Brit. M. J. 5004:1267 (1 Dec.), 1956.

A group of patients suffering from mild to moderate ulcerative colitis were treated by the introduction of hydrocortisone into the rectum by means of a slow drip. Treatment was given nightly, for two or three weeks. Twenty-one courses of treatment were given to 17 patients. In 14 instances, rapid clinical remission occurred, and in one, there was considerable improvement. All patients going into clinical remission showed an improved sigmoidoscopic picture, though the histological changes met with in small biopsy specimens did not in general show a corresponding improvement.

The effect of the treatment was not permanent, although a successful immediate outcome was usually followed by a period of clinical remission lasting at least for several months. In the case of four patients who suffered clinical relapse some months after an excellent response to treatment, the institution of a second course of treatment brought about clinical remission in a few days in three of them, so that repeated courses of treatment whenever symptoms recur may prove to be effective in some of those patients who respond to the first course of treatment.

It is possible that the symptomatic relief is due merely to lubrication of the colon, psychosomatic response to a new treatment, or an expensive form of systemic administration of hydrocortisone. However, the method used appears to be a useful addition to the treatment of ulcerative colitis, particularly as it can be carried out by patients in their own homes.

ARNOLD L. BERGER

CHRONIC FECAL IMPACTION IN CHILDREN: Gerald Mason Feiglen. California Med. 86:41-43 (Jan.), 1957.

Symptoms and findings associated with chronic fecal impaction as well as a method of treatment are discussed. Seventeen cases are reviewed and the disturbing influences

this problem presents for both parent and patient are considered.

Diagnosis was made by identifying the impaction on abdominal palpation and by digital examination after applying a topical anesthetic to the anal sphincter. Impacted stools are not necessarily hard—in some cases they are soft and gummy. Prior treatment by laxatives, enemas of different types gave only temporary relief. In 4 cases impactions had to be removed under general anesthesia. The author's suggested treatment involved topical, dietary, systemic and psychological methods. The specific treatment found most useful was the use of dioctyl sodium sulfasaccinate along with a flavored petrolatum, gradually stepped down and eliminated as the problem subsided. In all cases the chronic fecal impaction ceased and regular bowel habits were established.

ARTHUR L. KASLOW

FECALOMA TREATED WITH DIOCTYL SODIUM SULFOSUCCINATE: Harold C. Klein. Am. J. Digest. Dis. 2:37 (Jan.), 1957.

This is a report of a case of fecaloma of the sigmoid treated by giving 60 mg. dioctyl sodium sulfosuccinate capsule four times daily. Retention enemas of ½ ounce of a 1 per cent solution of the same drug in 4 ounces of water were administered daily. This medication helped to soften the fecal mass and small amounts of feces were passed daily for seven days, in this manner dissolving the fecaloma. This therapy prevented the necessity for surgical removal.

I. H. EINSEL

CHRONIC DIARRHEA: Editorial. Canad. M. A. J. 76:137 (15 Jan.), 1957.

Chronic diarrhea presents problems of diagnosis and if undiagnosed, therapeutic difficulties. The condition may be the result of systemic diseases such as adhesions, P. A., diabetes mellitus, thyrotoxicosis and uremia, or may be caused by lesions of the stomach, small intestines and colon. Diarrhea due to stomach diseases (achlorhydria, alcoholic gastritis and total gastrectomy) will result in watery stools which contain no blood, pus or mucus. Chronic diarrhea due to small and large bowel disease is generally caused by chronic ulcerative colitis, carcinoma of the rectum, regional enteritis, idiopathic steatorrhea, fistulas between segments of bowel and pseudomembraneous enterocolitis following the use of antibiotics. Diarrhea due to emotional human problems are generally intermittent and associated with stress.

A. J. BRENNER

DIVERTICULOSIS AND DIVERTICULITIS ROENTGEN FINDINGS AND THEIR INTERPRETATION: B. S. Wolf, M. Khilnani and R. H. Marshak. Am. J. Roentgeno. 77: 1957.

Diagnosis of chronic diverticulitis in the absence of a history and with previous acute episodes is difficult on the clinical grounds only. Clinical findings may be of such a minor character that a diagnosis cannot be made with certainty, however, there is stressed the importance of differentiating the signs of acute and chronic inflammation radiographically.

The roentgen findings of diverticulosis is characterized not only by the presence of multiple diverticula, but by haustral asymmetry and a somewhat flexible bowel. The flexibility of the bowel wall, however, being demonstrated by serial filming. The changes seen in the acute diverticulitis may consist of slight flattening of one wall, local spasm, irritability of the adjacent bowel and evidence of some edema in the mucosa. Occasionally, irregular eccentric defects may be demonstrated on the barium enema examination and these represent intramural type of an acute inflammatory process. Intramural defects, however, may persist for many years. On the other hand, chronic, indurated or proliferative diverticulitis shows thickening and contraction of the bowel wall with the mucosa pattern becoming distorted and exaggerated. The sinus and fistulous tracts are noted as well as pericolonic masses or abscesses. The suggestive working classification of diverticuli-

tis is brought forward: 1. acute diverticulitis with or without proliferation, 2. recurrent or multiple diverticulitis, 3. healed or sub-sided diverticulitis, single or multiple, 4. chronic diverticulitis with or without fistula or sinus formation.

V. J. GALANTE

DUODENAL INVOLVEMENT IN REGIONAL ILEITIS: T. E. Keats and R. Brady. Am. J. Roentgenol. 77:639, 1957.

The importance of this article stresses need to involve the upper alimentary tract since the duodenum may be involved in a regional ileitis, singly or in conjunction with the upper portion of the small intestinal tract. The findings of a regional enteritis of the duodenum do not differ from those associated with inflammation, mainly blunting, thickening and irregularity of the mucosal folds; later a disease with a polypoid appearance, due to island of hyperplastic mucosa; still later, with scarification and stenosis. The differential problem of a regional enteritis of the duodenum is peptic ulcer, lymphosarcoma, carcinoma of the duodenum, carcinoma of the ampulla of Vater, carcinoma of the pancreas with duodenal invasion, pancreatitis and hypertrophy of the Brunner's gland. Diagnosis is made with relative ease when the inflammation involves other portions of the intestinal tract. Three case presentations of regional enteritis involving the duodenum are present in this article.

V. J. GALANTE

BOOK REVIEWS FOR GASTROENTEROLOGISTS

PAPER ELECTROPHORESIS—CIBA FOUNDATION SYMPOSIUM: G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Elaine C. P. Miller, A.H-W.C., A.R.I.C., Editors for the Ciba Foundation. 224 pages, 74 illustrations. Little, Brown & Company, Boston, Mass., 1956. Price $6.75.

Blood chemistry until paper electrophoresis was introduced was one of the chief reliances in clinical diagnosis. This latter method has become an increasingly important diagnostic tool.

Not only in medicine but in the entire field of inorganic and organic substances, paper electrophoresis is employed in most branches of chemistry. For example, by combining electrophoresis and chromatography a simple way for a quantitative determination of amino acids has been opened up.

The determination of lipoproteins and glucoproteins has gained more and more importance. The evaluation of albumin/globulin ratio by paper electrophoresis has been used routinely as a supplement to the Van Slyke copper sulfate method for total protein.

Analysis of human hemoglobins by paper electrophoresis has been of great diagnostic value in fetal, adult and sickle-cell varieties.

Biochemists are urged to obtain this small but interesting volume on paper electrophoresis.

THE HAPPY LIFE OF A DOCTOR: Roger I. Lee, M.D. 278 pages, illustrated. Little, Brown & Company, Boston, Mass., 1956. Price $4.00.

This brilliantly written and related life story, his tribulations and rise to eminence in the medical profession by the author, should be read by all prospective medical students and physicians.

The reviewer enjoyed reading the book and congratulates Dr. Lee for his arduous work.

BONE STRUCTURE AND METABOLISM: G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc., Editors for the Ciba Foundation. 299 pages, 121 illustrations. Little, Brown & Co., Boston, Mass., 1956. Price $8.00.

An interesting and worthwhile book on the embryology and chemistry dealing with bone formation and growth. Anatomists and surgeons, especially orthopedic surgeons, will find valuable information relative to Vitamin D, parathyroid, Paget's disease, Gudek's atrophy and osteoarthritis of the hip.

CHIRURGIE DE L'ESTOMAC: R. Gueullette, Surgeon, Hopital de Paris. 584 pages, illustrated. Masson et Cie, Paris, France, 1956. Price 4,000 fr.

A beautifully bound and well printed volume dealing with surgery of the stomach.

Surgeons who read French will find valuable information in this monograph.

On page 567, the reader will find an excellent article on "Prolapse of the Mucosa into the Duodenum". An extensive index and chapter contents are found at the end.

PROCEEDINGS OF THE THIRD NATIONAL CANCER CONFERENCE, DETROIT, MICH., JUNE 4-6, 1956: Sponsored by the American Cancer Society, Inc. and National Cancer Institute, United Public Health Service. 961 pages, illustrated. J. B. Lippincott Company, Philadelphia, Pa., 1957. Price $9.00.

Physicians, whether they treat cancer or refer their patients to others, will find interesting and valuable information in this volume on cancer symposium.

The reviewer found a great many useful items which were unknown to him before reading the book.

J.A.M.A. CLINICAL ABSTRACTS OF DIAGNOSIS AND TREATMENT. Published with the approval of the Board of Trustees, American Medical Association, 564 pages. Intercontinental Medical Book Corporation with Grune & Stratton, Inc., New York, N. Y., 1957. Price $5.50.

Here is a book which all physicians will find helpful. Instead of cutting out an interesting abstract from the journal and filing it for future reference, in this cumulative volume the subject matter is arranged according to sections dealing with one of the systems. For instance, abstracts relating to the digestive tract will be found on pages 1 to 74 and the reader, who is interested in a particular reference, will find the exact page in the index.

It is highly recommended.

1956-57 YEAR BOOK OF GENERAL SURGERY: Evarts A. Graham, A.B., M.D., Emeritus Professor of Surgery, Washington University School of Medicine, etc., with a section on Anesthesia by C. Cullen, M.D., Professor of Surgery and Chairman of Division of Anesthesiology, State University of Iowa College of Medicine and Hospitals. 647 pages, illustrated. Year Book Publishers, Inc., Chicago, Ill., 1957. Price $6.75.

The Year Book of Surgery and Anesthesiology again brings to the physician's attention the best of the world's medical literature dealing with these specialties. The various abstracts appearing throughout the book plus the illustrations, bring valuable information of the latest methods for diagnosing and treating uncomplicated and complicated cases.

On page 81, neoplasms and their epidemology in the United States are discussed. More than 500,000 new cases of cancer are being diagnosed in this country each year. Page 94, environmental causes of cancer in man makes interesting reading.

OBESITY—ITS CAUSE, CLASSIFICATION AND CARE: E. Philip Gelvin, M.D., F.A.C.P., Associate in Medicine, New York Medical College, Flower Fifth Avenue Hospital, etc. and Thomas H. McGavack, M.D., F.A.C.P., Professor of Clinical Medicine, New York Medical College, Flower Fifth Avenue Hospital, etc. 146 pages. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, N. Y., 1957. Price $3.50.

This is an interesting, small but concise volume dealing with obesity. It is based on the experience gained at the Obesity Clinic at Metropolitan Hospital, New York, N. Y.

Diet, exercise and the use of drugs including thyroid and pituitary are discussed. The relation of endocrine factors to obesity is found only in a small number of cases.

Obesity in childhood, page 67, is rather short and should be elaborated, if and when a second edition is issued.

The reader's attention is called to page 109, where the authors discuss the relative merits of thyroid, anterior and posterior pituitary, sex hormones, 11-oxycorticoids and a diet of 125 gm. carbohydrates; 85 gm. proteins and 75 gm. fat (1,500 calorie diet).

An adequate bibliography and index complete the book. It is a useful reference book for the library of any physician.

The administration of Thorazine to cancer patients with marked relief of vomiting and intractable nausea as reported from the Montefiore Hospital is worthwhile trying when other remedies fail.

On page 327, Marcumar, an anticoagulant, is discussed, while on page 328, the lymphatic system and its ramifications make interesting reading.

Very interesting is the elevation of the serum amylase in various acute abdominal diseases on page 339. On page 340, the liver and spleen plus total right hepatic lobectomy for cancer of the gallbladder are discussed.

Cholecystography and intravenous cholangiography are included in the biliary tract section.

In the section on gastroenterology, the esophagus, stomach, bleeding from peptic ulcer, serum amylase in patients with acute perforation of gastroduodenal ulcers and nonoperative treatment of perforated peptic

ulcer, make interesting reading. The simplified technic using chymotrypsin lavage for cytologic diagnosis of gastric cancer should be tried on all patients before surgical approach.

Although primary malignant neoplasm of the duodenum is supposed to be a rarity, on page 446—31 cases are reported from the Mayo Clinic.

On page 537, the section on anesthesia, an adequate index and index of authors, complete the volume.

STONES OF THE MAIN BILIARY TRACT: Pablo L. Mirizzi, 162 pages, 79 illustrations, Masson & Cie, Paris, 1957. Price 2,200 Fr.

The book deals, as its title states, with stones in the common bile and hepatic ducts, their pathology, diagnosis and treatment. The author, Professor of Surgery at the University of Cordova, Argentina, is a pioneer in the field of operative cholangiography, which he introduced in 1931. The book covers therefore, more than 25 years of experience with operative cholangiography, which has become an indispensable step in the operation of gallstones, in Europe and South America much more than in the United States. Mirizzi uses 40 per cent iodized oil for cholangiography. He describes his technic in detail and provides many pictures of operative and postoperative cholangiograms, which are accompanied by detailed descriptions of the operative findings. The study of these illustrations makes careful reading of the book very worthwhile. The last part of the book discusses the surgical methods preferred by the author. He uses the transduodenal papillotomy only rarely, and prefers, apparently, as many European surgeons still do, the external choledochoduodenostomy. In the course of his writings Mirizzi quotes many authors whose names do not appear in the short bibliography. This should be corrected in the new edition. The illustrations are of an excellent quality. The book can be highly recommended to all those interested in gallstone diseases, internists, radiologists and surgeons alike.

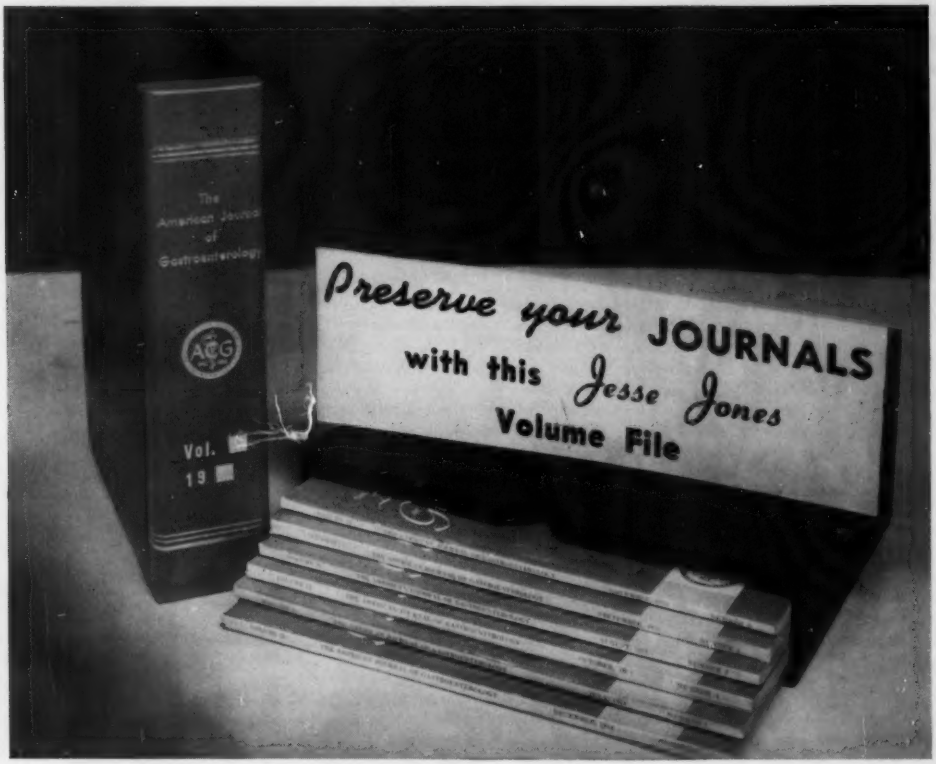
ANATOMICAL AND SURGICAL STUDIES OF THE LIVER: C. Couinaud, 530 pages, 256 illustrations, Masson & Cie, Paris, 1957. Price 4,500 Fr.

Until recently, resections of parts of the liver mostly of the left lobe, have been done only occasionally. There were no standardized hepatic lobectomies which could be compared to modern pulmonary lobectomies. Before the advent of planned hepaticolobectomies, detailed anatomical studies were necessary of the liver lobes and hilus structures, and most important, the intrahepatic divisions and subdivisions of bile ducts, portal veins, hepatic arteries and liver veins. In this admirable book, the author reports in full detail on his extensive anatomical studies covering the entire field of the divisions and subdivisions of the hepatic lobes and segments and all the hilum and intrahepatic distribution of the hilar structures and hepatic veins.

The second part of the book describes, step by step, hepatic lobectomies and segmentectomies with individual ligation of the structures concerned in these operations. Anatomical and surgical details are well illustrated. The book, because of its completeness, also will be of inestimable value to the increasing number of surgeons who, in the future, will do planned hepatic lobectomies and segmentectomies, once the field has been opened to the general surgeon. Special attention of this large group should be directed to the chapter on Surgical Treatment of Carcinoma of the Gallbladder. This may well be the beginning of a more hopeful era in the surgical treatment of this up to the present almost 100 per cent fatal disease. The surgical treatment of stones in the intrahepatic bile ducts will be made easier because of a better knowledge of the intrahepatic division of the hilus structures under guidance of the operative cholangiogram.

There are two bibliographies, one covering the anatomy and the second, the surgical literature. Europeans and American authors are quoted equally.

The book cannot be recommended highly enough. It has all the makings of becoming a standard text book on the subject of surgical anatomy and surgery of the liver.



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THE special world your little one lives in is only as secure as you make it. Security begins with saving. And there is no better way to save than with U.S. Savings Bonds. Safe—your interest and principal, up to any amount, guaranteed by the Government. Sound—Bonds now pay 3¼% when held to maturity. Systematic—when you buy regularly through your bank or the Payroll Savings Plan. It's so convenient and so wise—why not start your Savings Bonds program today? Make life more secure for someone you love.

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ACHROMYCIN*

Hydrochloride
Tetracycline HCl *Lederle*

THERAPEUTIC BLOOD LEVELS ACHIEVED IN MINUTES -- SUSTAINED FOR HOURS

Many physicians advantageously use the parenteral forms of ACHROMYCIN in establishing immediate, effective antibiotic concentrations. With ACHROMYCIN you can expect prompt control, with minimal side effects, over a wide variety of infections - reasons why ACHROMYCIN is one of today's foremost antibiotics.

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

*Reg. U. S. Pat. Off.

new paper[1] suggests 3 uses for DESITIN® ointment by colostomy patients

1 "In case of skin irritation around the colostomy" Desitin Ointment "under the dressing would be effective."

2 "to prevent possible stricture of the stoma at skin level" the patient should be taught to insert a gloved finger covered with Desitin Ointment.

3 The catheter used for irrigations "may be lubricated" with Desitin Ointment.

After ileostomy and colostomy Desitin Ointment affords *persistent* soothing, lubricant and healing properties in helping prevent, and clear up skin excoriation. Tubes of 1 oz., 2 oz., 4 oz., and 1 lb. jars.

WHY NOT REQUEST SAMPLES?

DESITIN CHEMICAL COMPANY
812 Branch Ave., Providence 4, R. I.

1. Breidenbach, L., and Secor, S. M.: Proper Handling of the Colostomy Patient, Amer. J. Surg. 93:50, 1957.

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Wyseals* / Equanil®

Wyeth
Philadelphia 1, Pa.

Meprobamate, Wyeth

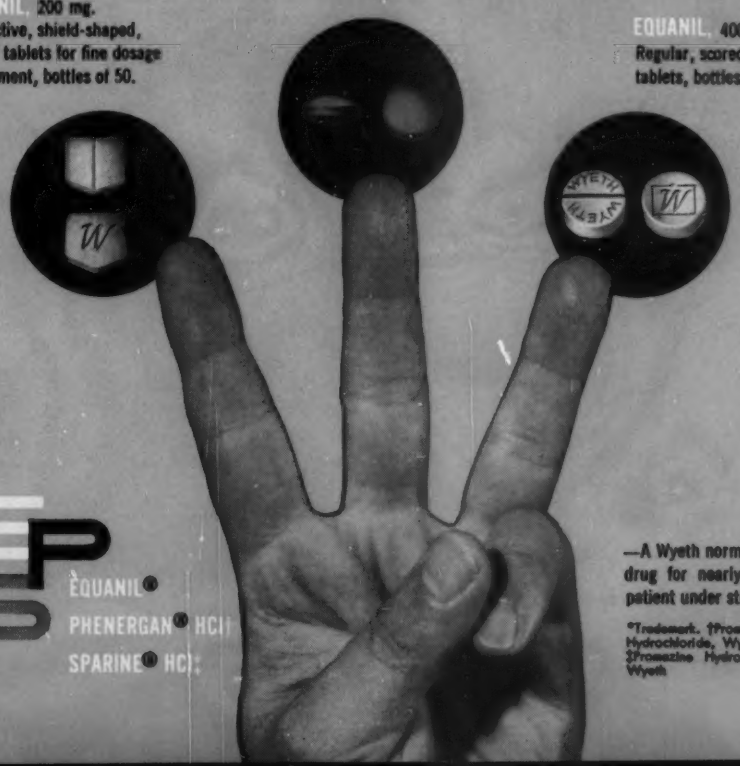
- Especially coated, easy to swallow
- Tranquilizer-conscious patients will not recognize new yellow tablets
- Different from regular 400-mg. and 200-mg. tablets
- Same indications, same dosage as original EQUANIL

NOW YOU HAVE A CHOICE OF 3 EQUANIL TABLETS

WYSEALS EQUANIL 400 mg.
Yellow tablets, bottles of 50.

EQUANIL 200 mg.
Distinctive, shield-shaped, scored tablets for fine dosage adjustment, bottles of 50.

EQUANIL 400 mg.
Regular, scored, white tablets, bottles of 50.



EQUANIL®
PHENERGAN® HCl†
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—A Wyeth normotropic drug for nearly every patient under stress

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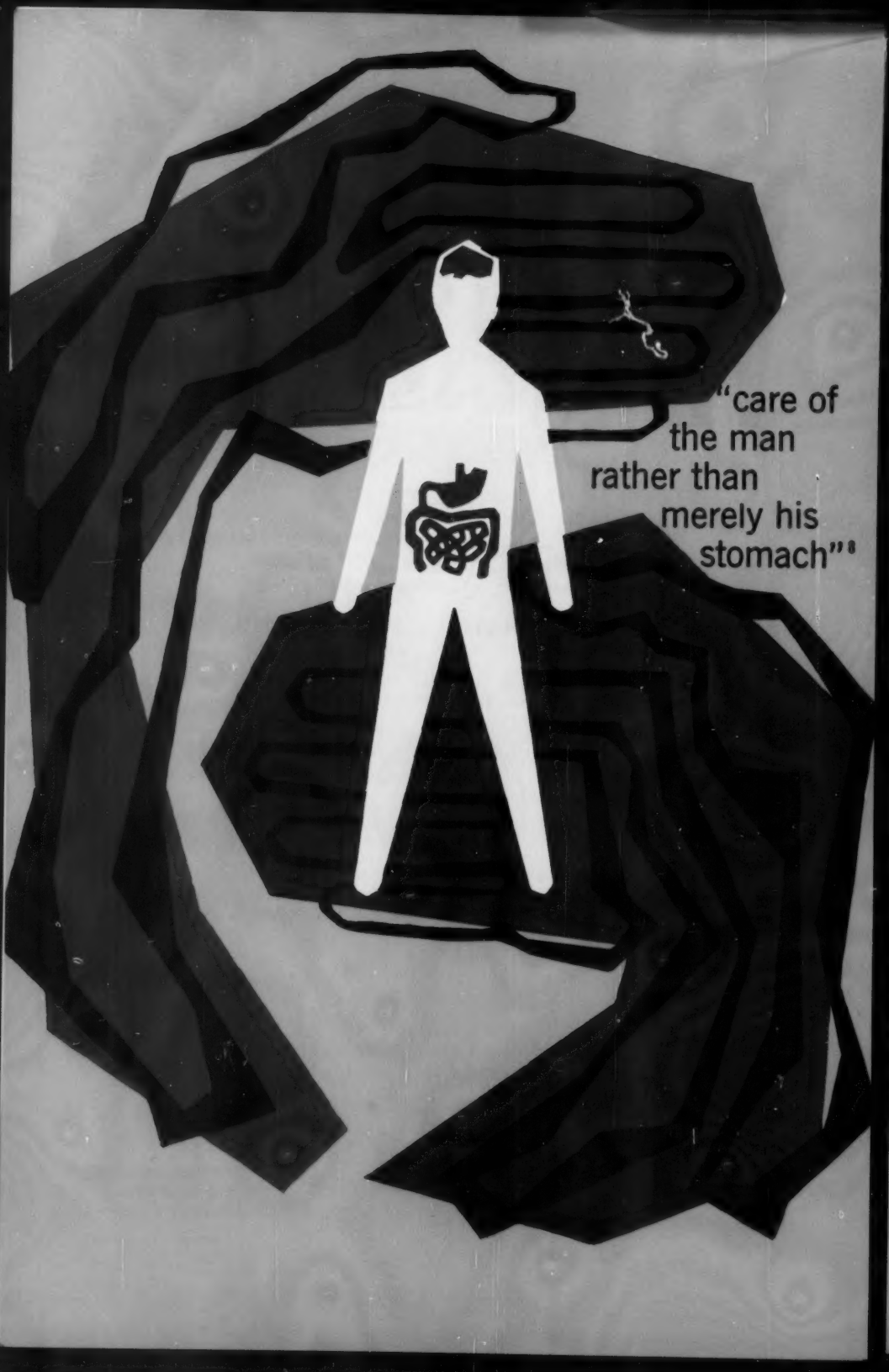
"care of
the man
rather than
merely his
stomach"[8]

"Milpath"

Miltown® + anticholinergic

two-level control of gastrointestinal dysfunction

at the central level

The tranquilizer Miltown® reduces anxiety and tension.[1,3,6,7]

Unlike the barbiturates, it does not impair mental or physical efficiency.[5,7]

at the peripheral level

The anticholinergic tridihexethyl iodide reduces hypermotility and hypersecretion.

Unlike the belladonna alkaloids, it rarely produces dry mouth or blurred vision.[2,4]

indications: peptic ulcer, spastic and irritable colon, esophageal spasm, G. I. symptoms of anxiety states.

each "Milpath" tablet contains:

Miltown® (meprobamate WALLACE) ..... 400 mg.
(2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate)

Tridihexethyl iodide ..... 25 mg.
(3-diethylamino-1-cyclohexyl-1-phenyl-1-propanol-ethiodide)

dosage: 1 tablet t.i.d. at mealtime and 2 tablets at bedtime.

available: bottles of 50 scored tablets.

references:

1. Altschul, A. and Billow, B.: The clinical use of meprobamate (Miltown®). New York J. Med. *57*:2361, July 15, 1957. 2. Atwater, J. S.: The use of anticholinergic agents in peptic ulcer therapy. J. M. A. Georgia *45*:421, Oct. 1956. 3. Borrus, J. C.: Study of effect of Miltown (2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate) on psychiatric states. J. A. M. A. *157*:1596, April 30, 1955. 4. Cayer, D.: Prolonged anticholinergic therapy of duodenal ulcer. Am. J. Digest. Dis. *1*:301, July 1956. 5. Marquis, D. G., Kelly, E. L., Miller, J. G., Gerard, R. W. and Rapoport, A.: Experimental studies of behavioral effects of meprobamate on normal subjects. Ann. New York Acad. Sc. *67*:701, May 9, 1957. 6. Phillips, R. E.: Use of meprobamate (Miltown®) for the treatment of emotional disorders. Am. Pract. & Digest Treat. *7*:1573, Oct. 1956. 7. Selling, L. S.: A clinical study of Miltown®, a new tranquilizing agent. J. Clin. & Exper. Psychopath. *17*:7, March 1956. 8. Wolf, S. and Wolff, H. G.: Human Gastric Function, Oxford University Press, New York, 1947.

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New Brunswick, N. J.

FIRST—clinically confirmed for better management of psychotic patients

NOW—clinically confirmed as an improved antiemetic agent

VESPRIN

Squibb Triflupromazine

PROMPT, POTENT and LONG-LASTING ANTIEMETIC ACTIVITY

Clinical investigators report that in clinical studies*

Post-operatively	After Nitrogen Mustard Therapy	In Chronic Nausea and Vomiting	In Infections, Intra-abdominal Disease, and Carcinomatosis	In Neurosurgical Diagnostic Procedures	In Pernicious Vomiting of Pregnancy

VESPRIN

- showed potent antiemetic action
- completely relieved nausea and vomiting in small intravenous doses
- showed a prolonged antiemetic effect
- caused little or no pain at injection site
- controlled chronic nausea and vomiting in orally administered doses
- produced relief in cases refractory to other antiemetics
- often markedly depressed or abolished the gag reflex
- terminated with singular effectiveness the hard-to-control nausea and vomiting common to nitrogen mustard therapy
- provided superior prophylaxis against the nausea and vomiting associated with pneumoencephalography

*Reports to the Squibb Institute for Medical Research

antiemetic dosage: *Intravenous route*—2 to 10 mg. for therapy or prophylaxis
Intramuscular route—5 to 15 mg. for therapy or prophylaxis
Oral route—Prophylactic doses may range from 20 to 30 mg. daily

supply: *Parenteral Solution*—1 cc. ampuls (20 mg./cc.)
Oral Tablets—10 mg., 25 mg., 50 mg., in bottles of 50 and 500

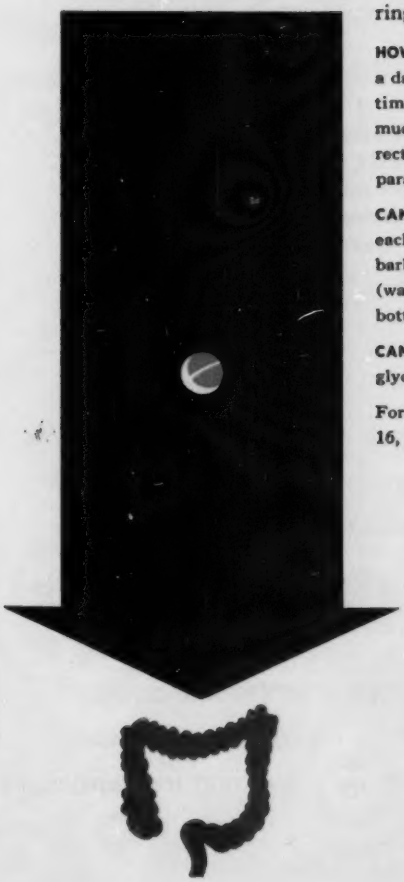
SQUIBB *Squibb Quality—the Priceless Ingredient*

effective, selective therapy

Cantil
for the colon

for functional and organic disorders

CANTIL relieves pain, cramps, bloating...curbs diarrhea...restores normal tone and motility. Selective action focused on the colon avoids widespread interference with normal autonomic function... minimizes urinary retention, mouth dryness, blurring of vision.



HOW CANTIL IS PRESCRIBED One or two tablets three times a day preferably with meals, and one or two tablets at bedtime for patients with ulcerative colitis, irritable colon, mucous colitis, spastic colitis, diverticulitis, diverticulosis, rectospasm, diarrhea following G.I. surgery, bacillary and parasitic disorders.

CANTIL—TWO FORMS CANTIL (plain)—25 mg. of CANTIL in each scored tablet—bottles of 100. CANTIL with Phenobarbital—25 mg. of CANTIL and 16 mg. of phenobarbital (warning: may be habit forming) in each scored tablet—bottles of 100.

CANTIL is the *only* brand of N-methyl-3-piperidyl-diphenylglycolate methobromide.

For more detailed information, request Brochure No. NDA 16, Lakeside Laboratories, Milwaukee 1, Wisconsin.

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NEW PATHIBA

combines **Meprobamate** *(400 mg.):*

Widely prescribed tranquilizer-muscle relaxant. Effectiveness in anxiety and tension states clinically demonstrated in millions of patients. Meprobamate acts only on the central nervous system. Does not increase gastric acid secretion. It has no known contraindications, can be used over long periods of time.[1,2,3]

with **Pathilon** *(25 mg.):*

An anticholinergic noted for its extremely low toxicity and high effectiveness in the treatment of G.I. tract disorders. In a comparative evaluation of currently employed anticholinergic drugs, PATHILON ranked high in clinical results, with few side effects, minimal complications, and few recurrences.[4]

Now...with **PATHIBAMATE**...*you can control disorders of the digestive tract and the "emotional overlay" so often associated with their origin and perpetuation...without fear of barbiturate loginess, hangover or addiction. Among the conditions which have shown dramatic response to* **PATHIBAMATE** *therapy:*

DUODENAL ULCER • GASTRIC ULCER • INTESTINAL COLIC
SPASTIC AND IRRITABLE COLON • ILEITIS • ESOPHAGEAL SPASM
ANXIETY NEUROSIS WITH G.I. SYMPTOMS • GASTRIC HYPERMOTILITY

AMATE*

Meprobamate with PATHILON® LEDERLE

Comments on PATHIBAMATE *from clinical investigators*

- "I find it easy to keep patients using the drug continuously and faithfully. I feel sure this is due to the desirable effect of the tranquilizing drug."[5]

- "The results in several people who were previously on belladonna-phenobarbital preparations are particularly interesting. Several people volunteered that they felt a great deal better on the present medication and noted less of the loginess associated with barbiturate administration."[6]

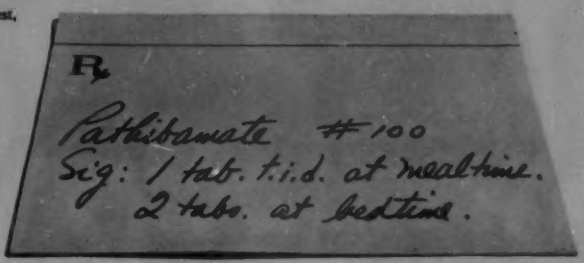
- PATHIBAMATE..."will favorably influence a majority of subjects suffering from various forms of gastrointestinal neurosis in which spasmodic manifestations and nervous tension are major clinical symptoms."[7]

- "In the patients with functional disturbances of the colon with a high emotional overlay, this has been to date a most effective drug."[5]

References: 1. Borrus, J. C.: *M. Clin. North America*, in press, 1957. 2. Gillette, H. E.: *Internat. Rec. Med. & G. P. Clin.* 169:453, 1956. 3. Pennington, V. M.: *J.A.M.A.*, in press, 1957. 4. Cayer, D.: Prolonged Anticholinergic Therapy of Duodenal Ulcer. Am. J. Dig. Dis. 1:301-309 (July) 1956. 5. McGlone, F. B.: Personal Communication to Lederle Laboratories. 6. Texter, E. C., Jr.: Personal Communication to Lederle Laboratories. 7. Bauer, H. G. and McGavack, T. H.: Personal Communication to Lederle Laboratories.

Supplied: Bottles of 100 and 1000

Administration and Dosage: 1 tablet three times a day at mealtimes and 2 tablets at bedtime. Full information on PATHIBAMATE available on request, or see your local Lederle representative.



Lederle LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

*Trademark ®Registered Trademark for Tridihexethyl Iodide Lederle

Resion stops diarrhea quickly

Resion acts instantly in the intestinal tract

by the unique electrochemical adsorptive action (anion exchange) of its resin component.[1] Insoluble and nontoxic[2], Resion removes noxious substances through electrochemical attraction—like a magnet. This action occurs instantaneously . . . as quickly as Resion and toxic acid molecules are within functioning range of chemical forces[1], —yet it leaves important amino acids, vitamins and minerals unaffected. With Resion, 86 of 90 patients had complete relief of diarrhea in 8 to 12 hours.[3]

For simple diarrhea: Resion, a combination of polyamine methylene resin and synthetic silicates.

For infectious diarrhea: Resion P-M-S, the Resion formula plus polymyxin, phthalysulfacetamide and the parabens.

References: 1. Martin, G. J.: Ion-Exchange and Adsorptive Agents in Medicine, Little, Brown and Co., Boston, 1955, P. 205. 2. Lichtman, A. L.: Exper. Med. & Surg. 9:90, 1951. 3. Gabroy, H. K., and Selsman, G. J. V.: Amer. J. Digest. Dis. 20:395, 1953.

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when he smokes too much . . .

Whenever indigestion results from habitual overdoing in any form (excess of cigarettes or alcohol, dietary indiscretion, nervous tension), symptoms can be quickly alleviated night and day with Gelusil and the new formulation Gelusil-Lac.

To avoid daytime distress: Gelusil provides the sustained action of magnesium trisilicate and specially prepared aluminum hydroxide gel to restore and maintain gastric pH within normal range. Because it does not overneutralize or alkalize, Gelusil avoids the twin dangers of acid rebound and systemic alkalosis.

To prevent middle-of-the-night attacks: In Gelusil-Lac, the proven antacid action of Gelusil is combined with sustained buffering effect of specially prepared high protein (low fat) milk solids to prevent gastric pain at night.

Nonconstipating: The specially prepared aluminum hydroxide component in Gelusil has a low order of chemical activity. Thus formation of astringent – and constipating – aluminum chloride is minimal.

Dosage: 2 Gelusil tablets or 2 teaspoonfuls Gelusil liquid two hours after eating or when symptoms are pronounced. Each tablet or teaspoonful provides: 7½ gr. magnesium trisilicate and 4 gr. aluminum hydroxide gel. Gelusil-Lac: At bedtime, one heaping tablespoonful stirred rapidly into one-half glass (4 fl. oz.) of cool water. (Provides equivalent of 4 Gelusil tablets.)

Gelusil®/Gelusil-Lac

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100 YEARS OF SERVICE TO THE MEDICAL PROFESSION